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DERMATOLOGICAL CHANGES IN HYPOCALCAEMIA.

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Though many published case-reports of diseases associated with hypocalcaemia refer to skin changes, British dermatologists have tended to be sceptical of the suggested rôle of calcium deficiency in skin disease. The majority of dermatological text-books in English make little reference to calcium deficiency, though Wiener (1947) devotes a section to hypoparathyroidism. The skin changes associated with hypocalcaemia may be more familiar to those who treat endocrine and metabolic disease. The present series of cases is thought to be worth reporting, since the nail and hair changes sometimes preceded other clinical manifestations of hypocalcaemia and their significance was not realized until tetany ensued.

Since hypocalcaemia without other known deficiencies occurs in hypoparathyroidism, the latter disease will be reviewed first and five cases reported. Twenty-nine cases of steatorrhoea will then be summarized, two cases being reported in detail. Steatorrhoea causes malabsorption of calcium as well as of iron and fat-soluble vitamins so that the skin changes cannot be attributed with confidence to any particular deficiency, especially since the blood electrolyte levels tend to be maintained at the expense of the tissues, and so do not provide an accurate index to the nutritional status of the tissues. Nevertheless it is worth comparing the skin changes in steatorrhoea with those of hypoparathyroidism. The two cases of steatorrhoea reported in detail are those in which the changes were observed to occur immediately after attacks of tetany.

Case Reports.

Case 1 : Idiopathic Hypoparathyroidism.

A boy aged 9 years.

Epileptic fits with occasional spasms of tetany started at 5 years of age (full clinical details of this and the following case are reported elsewhere—Simpson, 1952).

When first seen at 9 years of age (1949) the skin was dry and slightly scaly. The finger-nails were brittle, cracked longitudinally, and showed transverse white patches (Fig. 1). The hair was normal. Dental development was markedly delayed and the enamel of the incisor teeth was transversely ridged (Fig. 2). The roots of some of the teeth were shortened (skiagram). Serum calcium was 5·0 mg. % and serum inor-

FIG. 1.—Case 1 : Idiopathic hypoparathyroidism. Leuconychia and onychorrhexis with longitudinal splitting.

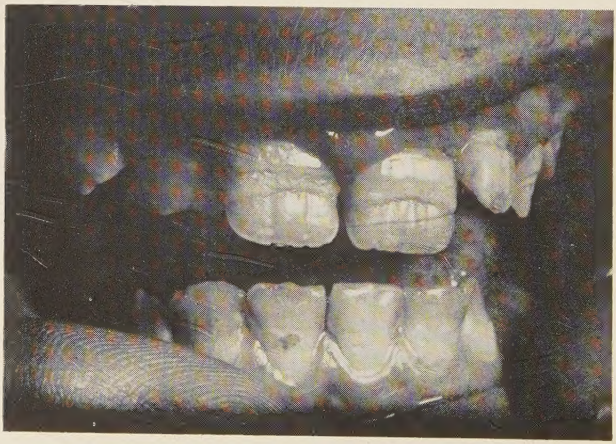


FIG. 2.—Case 1 : Furrowing of incisor teeth.

ganic phosphate 6·4 mg. % despite positive calcium balance and normal fat balance. Treatment with calcium lactate and calciferol rapidly restored the blood chemistry to normal and abolished epilepsy and tetany. The skin became normal in appearance and onychorrhexis disappeared though leuconychia remained. The skin and nail changes reappeared when the serum calcium subsequently dropped, but no critical level was observed. Relapses tended to occur in the winter. In 1952, the third year of treatment, the serum calcium fell to 7·5 mg. %. Onychorrhexis became severe

nd a small bulla, about 1 cm. in diameter, appeared on the skin over the left hypochon-lrium. It was non-itchy and painless. Unfortunately he did not report it until a veek later when it was covered with a scab. There was no systemic disturbance nd no secondary lesions occurred. When the scab separated it left a pink scaly nacule with an oval brown margin (1 × 1·5 cm.).

No transverse grooving of the nails was noted in this patient and no fungus was solated from nail scrapings.

Case 2 : Idiopathic Hypoparathyroidism.

A woman aged 46 years.

Symptoms of tetany occurred intermittently from the age of 28 years. During evere attacks the scalp hair was shed but it regrew when tetany was controlled. The kin and hair were normal when she first came under observation in March 1949, ut the finger-nails were longitudinally striated, brittle, and split along the free edges. There was no leuconychia and no fungus infection. Serum calcium was 7·0 mg. %, erum inorganic phosphate 4·5 mg. %, and the blood chemistry was otherwise normal. She had previously had bilateral lenticular extraction for cataract and all teeth had been extracted. Tetany disappeared after treatment (calcium gluconate and calciferol) nd the nails returned to normal.

In February 1951 her serum calcium fell again to 7·7 mg. % and she developed a kin lesion at the base of the neck, upper sternum and shoulders.

Dr. Herbert Brown and Dr. James Sommerville kindly examined the patient and greed that the appearance was unique. Dr. Sommerville described mild fading dis-rete folliculo-vesicular pinhead-size lesions which were drying up and showed a ten-lency to scale. The lesions were light purplish red in colour. The skin of the upper runk was not all greasy and the eruption did not suggest a seborrhoeide. Unfor-unately the lesion was fading when photographed. She stated that it had recurred very winter for several years.

Case 3 : Post-thyroidectomy Hypoparathyroidism.

A woman aged 36 years.

After operation for nodular goitre in March 1952 tetany developed with depression of serum calcium to 4·0 mg. % and elevation of serum inorganic phosphate to 7·8 mg.%.

FIG. 3.—Case 3 : Post-thyroidectomy hypoparathyroidism. Grooving of nails of first three fingers.

During the period of hypocalcaemia the scalp hair became brittle and lustreless and was shed in large quantities. The eyebrows became scanty and the skin of the face dry, scaly and slightly pigmented. Four to six weeks after operation the lunulae of the nails of the first and second fingers of both hands were grooved, and later the third fingers were also affected (Fig. 3). Four months after operation, when the serum calcium was normal (after treatment with calcium lactate and calciferol), the growing part of the nails was normal and hair was no longer being shed. This improvement has been maintained. There is now (June 1953) no abnormality. Thyroid function is normal.

Case 4 : Post-thyroidectomy Hypoparathyroidism.

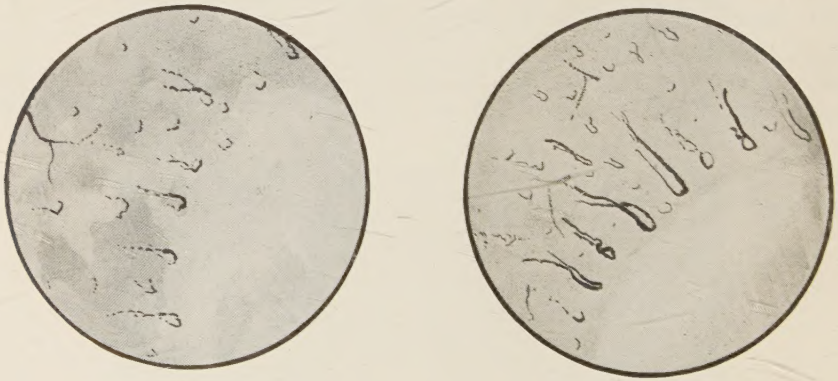
A women aged 69 years.

Tetany developed in March 1952 after subtotal thyroidectomy for non-toxic thyroid adenoma suspected of malignancy. The serum calcium fell to 5·7 mg. % and the serum inorganic phosphate rose to 5·4 mg. %. Slight hollowing of the lunulae of the thumb-nails was first observed ten weeks later and further grooves developed during the next month. No skin or hair changes were observed. Treatment with calcium lactate and calciferol caused rapid recovery from tetany and no further dermatological lesions have developed. One year later the blood chemistry remained normal when treatment was gradually withdrawn. No signs of myxoedema have been noted.

Case 5 : Parathyroid Adenoma.

A woman aged 58 years.

Tetany developed after removal of a mediastinal adenoma of a parathyroid gland in November 1952 in a typical case of osteitis fibrosa generalisata in which no dermatological lesion was present. With depression of serum calcium to 7·2 mg. % she developed paraesthesiae of the face and fingers and signs of latent tetany (Simpson, 1952),



(*a*) (*b*)

FIG. 4.—Case 5 : Hypoparathyroidism after parathyroidectomy for adenoma. (*a*) Drawing of nail-fold microscopic appearance during latent tetany with paraesthesia. The capillaries are constricted, particularly the efferent limb of the loops. (*b*) Normal capillary loops after control of tetany.

but frank tetany was prevented by treatment with calcium lactate and calciferol. The skin became dry, the lips cyanosed, and the ankles oedematous (probably due to mild cardiac failure, as the oedema was hypostatic). Scalp hair became dry, brittle, and began to fall out. In December 1952, when paraesthesia was marked and Chvostek's and Trousseau's signs present, the nail-bed of the fingers was examined with a

binocular microscope. The capillary loops were very narrow and the efferent limb was incomplete (Fig. 4(*a*)). This was confirmed on subsequent examinations. Two weeks later (24 days after operation) the lunulae of both thumb-nails were observed to be growing in rough and hollowed. Paraesthesia was now absent, Trousseau's sign could not be elicited, nerve accommodation was normal, and Chvostek's sign only slightly positive. Microscopy at that time showed normal capillary loops in the nail-beds (Fig. 4(*b*)). Further grooving of the nails occurred until February 1953. In May the skin was less dry and scalp hair was beginning to grow again. No pigmentation has occurred.

Case 6 : Idiopathic Steatorrhoea.

A woman aged 32 years.

After eight months of progressive asthenia and occasional diarrhoea this patient was admitted to hospital with tetany in April 1952. Serum calcium was 4·3 mg. % serum inorganic phosphate 3·0 mg. %, and a fat balance showed defective fat absorption. The skin was dry, inelastic, scaly and pigmented on the cheeks and hands.

Fig. 5.—Case 6 : Idiopathic steatorrhoea. Dry, scaly skin, slightly pigmented. Eyebrows thinned.

Scalp and eyebrow hair was thin and the thumb-nails showed transverse grooves. The nail folds were ragged (Figs. 5 and 6). The lips were fissured and the tongue was slightly atrophic. Further deep transverse grooves appeared in the thumb-nails 3–4 weeks after attacks of tetany. Response to treatment with calcium lactate, calciferol, and a low fat diet was slow. Signs of latent tetany did not disappear until July 1952 : at that time nail and hair growth became normal and pigmentation disappeared from the hands but not from the face. In October 1952 the serum calcium dropped again, paraesthesia reappeared, and further nail-grooving occurred in the thumbs, and later in the second and third fingers. This once more cleared up when treatment was increased.

Case 7 : Coeliac Disease.

A woman aged 19 years.

This patient has had steatorrhoea since coeliac disease developed at 3 years of age. Tetany occurred (with serum calcium 7·0 mg. %) at intervals from 1946 when she was aged 13 years. Since the onset of coeliac disease the finger-nails had been

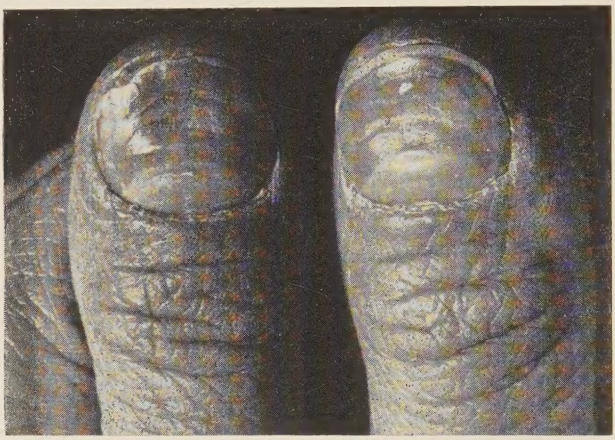


Fig. 6—Case 6 : Transverse grooving of thumb-nails.

broad, deformed, and brittle. At a later (indefinite) date they became greatly thickened (Fig. 8). No fungus was detected in nail scrapings in January 1949, but epidermophyton and a few colonies of aspergillus niger were later isolated in culture. The scalp and eyebrow hair was almost completely shed after tetany started (Fig. 7). Histology of the skin of the vertex was normal. The skin was moist, elastic, and not abnormally pigmented. Apart from a transient rash in 1948, of which no details are available, she has had no skin lesion except chilblains of the legs in winter. Satisfactory control of this patient's serum calcium has never been established. The nails remain unchanged, but there appeared to be a little hair growth in December 1952.

Cases 8–34 : Steatorrhoea.

These 27 cases, with cases 6 and 7, are summarized in Table I. Tetany was present in 5 cases and osteomalacia or rickets in 5 others. In many cases the serum calcium was not recorded. In the others it varied from 7·0 to 9·5 mg. %.

Table I.

Steatorrhoea proved	29 cases
Skin dry, inelastic	10 ,,
Pigmentation	17 ,,
Psoriasis	3 ,,
Herpetic and bullous eruptions	2 ,,
Urticaria	2 ,,
Perniosis	2 ,,
Bruising	2 ,,
Multiple papillomata	1 ,,
Scalp hair changes	4 ,,
Loss of body hair	2 ,,
Nail changes	5 ,,
Fungus infections	1 ,,
Clubbed fingers	7 ,,

Review of the Literature.

The skin, in cases of idiopathic hypoparathyroidism, is usually dry, rough, puffy, and scaly (Cantarow, 1932). Pigmentation is also common (Hoffmann, 1896 ; Foerster, 1916 ; Cantarow, 1932 ; Lachmann, 1941), though less so than in steatorrhoea. Dermographia and localized areas of puffiness of the

Fig. 7.—Case 7 : Coeliac disease. Loss of scalp and eyebrow hair. Skin normal.

skin or frank oedema are reported, usually limited to the face or the dorsa of the hands and feet, but sometimes generalized (Cantarow, 1947 ; Levy, 1947). This occurs more frequently in infants and is attributed to increased capillary permeability. Localized skin lesions of unusual nature are noted in idiopathic hypoparathyroidism, and, as in Case 2 of the present report, may have a seasonal recurrence. Learner and Brown's case (1943) started with a vesicular eruption which later developed sharply marginated solid purplish-red patches of thickened skin covered with loose flaky scales. There was no evidence of mycotic infection. Cheilitis and glossitis were also present. The lesions

cleared after treatment with calcium and calciferol. This was also the experience of Cantarow, Stewart and Morgan (1939). The few cases reported seem to be similar in nature as far as can be judged from clinical description and published photographs. A scaly patch starting with a vesicular lesion, as in the first two cases of the present series, is usually described, but no single author has described more than one or two cases, so that the difficulty in pronouncing

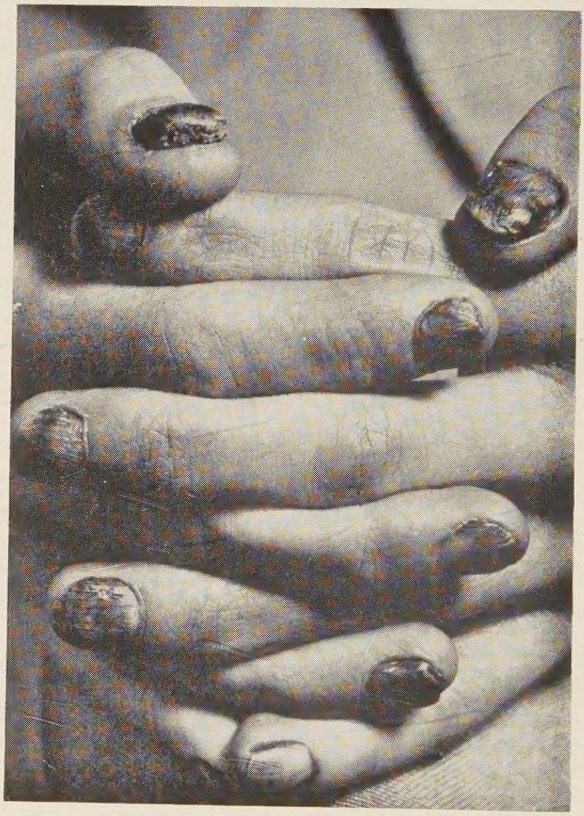


FIG. 8.—Case 7 : Mycotic infection of nails.

the lesions identical will readily be appreciated ; and it is not possible to state whether these localized lesions are specific to idiopathic hypoparathyroidism. They are not mentioned in Wiener's (1947) short chapter on the subject. The writer has not traced reports of similar skin changes in hypocalcaemia due to other causes.

Impetigo herpetiformis of Hebra is the only well-defined syndrome which has been related to hypocalcaemia. Since the early reports of Schardon (1921) and Walter (1922) many cases of this association have been recorded. They are reviewed by Wiener (1947). To his cases may be added those reported by

Lachmann (1941), Engefeldt and Gentele (1950), Beek (1951) and Ferriman (1953). The herpetic bulla noted in a typical position in Case 1 did not spread and no systemic disturbance occurred ; it was not considered to be impetigo herpetiformis. Two cases of steatorrhoea showed herpetic lesions. One (with serum calcium 7·1 mg. %) was thought to be zoster ; the other (with serum calcium 8·8. mg. % in steatorrhoea following jaundice) was believed to be dermatitis herpetiformis. Lachmann (1941) and Wiener (1947) draw attention to the clinical similarity between impetigo herpetiformis of Hebra and pustular psoriasis, in which they believe that hypocalcaemia is an aetiological factor. Lachmann (1941) believes that both syndromes are related to acrodermatitis continua (Hallopeau). Impetigo herpetiformis is also found in association with disturbances of other endocrine glands (Bartmann, 1937), though many workers believe that in these cases, too, there is disturbance of calcium metabolism.

Skin changes are frequently seen in steatorrhoea, and indeed may be the cause of the patients' seeking medical advice in a high percentage of cases (Cooke, 1952). In Cooke's experience the principal lesion is " seborrhoeic dermatitis," a desquamating type of rash affecting the hands, forearms, legs, and occasionally the face. He also found a relatively high incidence of lesions simulating psoriasis, often appearing only when the patient was markedly debilitated. In the present series (Table I) it occurred in only three of twenty-nine cases. Pigmentation occurs in the majority of cases of steatorrhoea. It may be generalized or confined to exposed surfaces, where it resembles pellagra (Cooke, Peeney and Hawkins, 1953). Most often in the present series it gave the face and hands an " unwashed " appearance or resembled a normal sun tan ; but it varied from a pale yellow tint to pigmentation sufficiently dark to suggest a diagnosis of Addison's disease, though buccal pigmentation was never seen. Similar changes occur in tropical sprue. The similarity of the skin changes in steatorrhoea to those of hypoparathyroidism is marked. One cannot confidently attribute them to calcium deficiency, though serum calcium levels as low as 7·0 mg. % were found in cases in this series and many showed bone changes indicative of prolonged negative calcium balance. Multiple vitamin, electrolyte and fatty acid deficiencies occur in steatorrhoea. Certainly cheilitis, glossitis and haemorrhagic manifestations can best be explained by malabsorption of vitamins B-group, C, and K. Steatorrhoea is, however, included in this review, as the acute changes after tetany are well seen in this condition. Calcium deficiency is stated to be a cause of purpura (Owen, 1950), but in view of the very small amount of calcium required to maintain blood coagulation (Stefanini, 1950) it is unlikely that bleeding will result from hypocalcaemia *per se*.

The relation of other skin diseases to calcium metabolism is less well established. Mamou (1932) considered that scleroderma was due to parathyroid

deficiency, though many others have believed it to be the result of hyperparathyroidism and claimed improvement after parathyroidectomy (Wiener, 1947). Thro and Ehn (1920) claimed that they found low blood calcium in furunculosis, and raised blood calcium in acne and sycosis barbae, but their work has not been confirmed. Parathyroid insufficiency has also been thought to be present in eczema (Winterstein, 1935 ; Holtz, 1936 ; Schmidt-la Baume 1937 ; Plügge, 1938) but here, too, the evidence is not convincing.

Nail Changes.

Abnormalities of the nails and hair are more consistently found in hypocalcaemia than are skin changes and can be more directly correlated with the serum calcium level. Leuconychia has been popularly associated with " calcium deficiency." It was found only in Case 1 (Fig. 1), the child with idiopathic hypoparathyroidism, and was unaffected by treatment. On the other hand, the longitudinally striated brittle nails tending to split at the free edge (onychorrhexis), which was observed in both cases of idiopathic hypoparathyroidism, disappeared when the serum calcium was restored to normal and reappeared when relapse occurred. Similar nail changes are mentioned in most reported cases. The finger- and toe-nails of a boy aged 15 suffering from this disease were short, thick, and largely overgrown by skin (Emerson, Walsh and Howard, 1941). These authors state that the appearance of the nails was suggestive of epidermophytosis. Monilial infection of the nails (and occasionally of the mouth) has been reported in many cases of idiopathic hypoparathyroidism (Thorpe and Handley, 1929 ; Cantarow, Stewart and Morgan, 1939 ; Drake, Albright, Bauer and Castleman, 1929 ; Sevringhaus, 1942 ; Talbot, Butler and McLachlan, 1943). As moniliasis sometimes preceded other clinical evidence of hypoparathyroidism, Sutphin, Albright and McCune (1943) have considered it to be of importance in the causation of the glandular disease. In the present series no fungus infection was detected in any case where hypocalcaemia was due to parathyroid deficiency but in one case of steatorrhoea with chronic tetany (Case 7, Fig. 8) the nails were infected with epidermophyton and aspergillus. In the writer's opinion it is more probable that chronic hypocalcaemia leads to ectodermal dysplasia, which renders the nail more susceptible to infection in the same way as the atrophic nails caused by thromboangiitis obliterans (Allan, Barker and Hines, 1946).

The nail changes in the three cases of post-operative hypoparathyroidism (Fig. 3) were unlike those of the idiopathic disease and were identical with those following tetany in a case of steatorrhoea (Fig 6). In these cases the nails became brittle and transversely grooved. Similar changes are reported in many of the papers reviewed. The grooves appeared at the base of the nail about a month after attacks of carpal spasm or of severe paraesthesia.

In one case the nail-beds were examined at intervals from the time of removal of a parathyroid adenoma. When signs of latent tetany were present the capillary loops in the nail-beds showed spasm of the efferent limb. This disappeared when the blood calcium level was restored and signs of latent tetany disappeared (Fig. 4). One month later the growing margin of the nail showed typical grooving. In the four cases showing transverse grooving after tetany it appeared first in the thumb-nails and disappeared last from that site. The second and third fingers were next most commonly affected. Although the toe-nails became brittle, grooving was not seen, possibly due to the absence of pedal spasm. Unfortunately Case 2 was not seen after her attacks of carpopedal spasm. Case 1 had very few spasms, most of his tetanic fits being epileptiform (Simpson, 1952).

Thin, brittle, deformed nails, often hollowed, are common in steatorrhoea even in the absence of tetany. As iron deficiency is so commonly present it is not possible to attribute them to calcium deficiency though this may be an added factor.

Hair Changes.

Transient loss of scalp hair was seen in all cases of hypoparathyroidism following attacks of tetany except in Case 1, and in at least two of the five cases of steatorrhoea in which manifest tetany occurred (Figs. 5, 7). This was previously observed by Hoffman (1896), Leischner and Köhler (1911), Learner and Brown (1943), and Rundle (1951). The remaining hair was brittle and lacked lustre. The hair may cease growing without actually becoming scant (Foerster, 1916). In hypoparathyroidism the hair is often thin and patchy on the head, absent in the axilla and pubes, and scanty in the eyelashes and eyebrows (Emerson, Walsh and Howard, 1941 ; Albright and Reifenstein, 1948), but these changes are also common in steatorrhoea (Table I) ; and in the latter the scalp hair is often fine and silky with early greying (Cooke, 1952 ; Cooke, Peeney and Hawkins, 1953), which again might be due to iron deficiency.

Other Ectodermal Changes.

It is beyond the scope of this paper to discuss in detail the further changes occurring in ectodermal tissues as the result of hypocalcaemia, but they will be described briefly as they are of great diagnostic assistance. Fuller information can be obtained in the monographs by Shelling (1935), and by Albright and Reifenstein (1948). Cataract of the eye lenses is one of the most constant features of chronic hypocalcaemia, whatever its aetiology, and should always be looked for. Dental changes are found only if hypocalcaemia exists before complete formation of the teeth. Case 1 (Fig. 2) is an excellent example, showing transverse furrowing of the incisors. These changes are presumably of

similar nature to the nail-furrows as they occur at growth periods during which tetany is present (Falta, 1923). Radiology shows hypoplasia of the roots of those teeth which develop after the onset of hypoparathyroidism.

Discussion.

This account suggests that the dermatological manifestations of hypocalcaemia fall into three classes :

(1) Abnormalities of growth of hair and nails associated with latent or manifest tetany.

(2) Skin, nail and hair changes associated with prolonged hypocalcaemia.

(3) Secondary infection of skin and nail.

Acute Hypocalcaemia causes temporary disturbance of growth of ectodermal tissue, resulting in shedding of the hair, grooving of the nails, and possibly furrowing of the developing dental enamel. These changes are more likely to be present if tetany occurs, though actual carpo-pedal spasm is unnecessary. Leischner and Köhler (1911) and Shelling (1935) noted shedding of the nails and necrosis of the nail beds in hypoparathyroidism and suggested that angiospasm was responsible. Jang (1940) and Harvey and Lilienthal (1942) have recorded an increased susceptibility to angiospasm in tetany, but Case 5 of the present report is the first documented case in which the development of angiospasm of the nail-fold with subsequent grooving of the underlying nail has been observed. The microscopic appearance was exactly comparable with that seen in Raynaud's disease (Allan, Barker and Hines, 1946), in which, as in chronic ischaemia from thromboangiitis obliterans, nail atrophy occurs. Lewis and Pickering (1936) attributed the impaired skin and nail nutrition commonly seen in nervous diseases, such as syringomyelia, to poor circulation. Conversely, improved circulation in ischaemic vascular disorders is reported after calcium gluconate injection (Weischel, 1940), high calcium diet with calciferol supplements (Bernheim and London, 1932) and injections of parathyroid extract (Conwell, 1933).

The transverse furrowing of the nails known as Beau's lines, seen in so many acute diseases, may have the same causation but this is not necessarily so. In one case of this series steatorrhoea was minimal but protein absorption inadequate. The serum calcium was moderately depressed (8·0 mg. %) but plasma proteins were very low. Her nails showed typical Beau's lines (Fig. 9). On a high protein diet her nail furrowing disappeared completely though the serum calcium remained low, and when the lines reappeared the serum calcium had risen to a normal level as the result of treatment with calciferol.

Angiospasm with tissue ischaemia may explain the rapid shedding of the hair. Wright (1929) has suggested that alopecia occurring in " neuropathic " cases may be so explained.

Chronic Hypocalcaemia offers a more difficult problem. The oedema found in children with hypoparathyroidism is attributed to increased permeability of blood vessels, with angiospasm (Cantarow, 1947). The nature of the other changes is less certain. Nutritional deficiencies, whether primary or secondary to malabsorption, tend to be multiple, but " pure " calcium deficiency is seen in hypoparathyroidism. In that state the most constant changes are dryness, puffiness, scaliness, and pigmentation of the skin, brittleness with longitudinal striation of the nails, and scantiness of scalp, eyebrow, and axillary hair. Most of these features are also seen in steatorrhoea, but a trophic function of the parathyroid gland cannot be excluded. The skin and hair resemble

FIG. 9.—Malabsorption syndrome with hypocalcaemia and hypoproteinaemia. Beau's lines on thumb-nails.

those of myxoedema though puffiness is less marked. Similarly the onychorrhexis resembles that found in many cases of anaemia and in senile atrophy. Magnesium deficiency in animals leads to a tetanic state, and disturbances of hair and nails surprisingly similar to those caused by calcium deficiency (Orent, Kruse and McCollum, 1932) or by parathyroidectomy (Bandler, 1920). Thus the end-effects of different deficiency diseases are very similar. The traces of calcium, iron and magnesium in the skin and nails are required for enzymatic processes. Interruption of protein synthesis at different points in the chain would lead to similar end-results. For this reason the author thinks that analysis of nail protein is of no value. Emerson, Walsh and Howard (1941) found that the cystine content of the nails was reduced in one of their cases of hypoparathyroidism, and suggested further investigation of the sulphur metabolism. The author has not succeeded in getting reliable results in assaying the cystine content of nails by chemical methods, and unfortunately this amino-acid tends to decompose greatly during paper chromatography (Dent, 1951).

Dent points out (personal communication) that it is unlikely that the amino-acid structure of the protein would vary. Since, if the above hypothesis be accepted, the end effects on protein anabolism would give no clue to the site of enzyme block it has not seemed worth pursuing this question further. Calcium is well known as an activator of many enzyme reactions. It is also known to decrease cell permeability (Osterhout, 1922), increase protoplasm viscosity and elasticity (Fauré-Fremiet, 1929), reduce fluid imbibition by protoplasm (Gellhorn, 1929), and enhance the repair of damaged cell surfaces (Chambers, 1926). It is not surprising that prolonged deficiency leads to changes in the integument suggesting decreased growth and accelerated ageing of cells.

The place of the localized skin lesions noted only in idiopathic hypoparathyroidism cannot be adequately assessed from the few recorded cases. The seasonal recurrence suggests that they are related to the blood calcium level as the latter tends to drop in the winter. This type of lesion may be directly due to hormonal deficiency rather than to hypocalcaemia, but no physician sees enough of this rare disease to express a confident opinion. Unfortunately the author's patient (Case 2) refused a biopsy. It is to be hoped that single cases will be fully reported in future, with photographs.

Secondary Infection of defective skin or nail cells deprived of the effect of calcium in maintaining the integrity of their surface membrane may explain the third group of dermatological changes. The pathogenesis of impetigo herpetiformis of Hebra is unknown and no virus has been incriminated, but some unknown pathogenic agent acts on a skin rendered less resistant by parathyroid or other hormonal deficiency. The mycotic infections of the nails are also attributable to this factor. In the only case in the present series the fungus infection long preceded symptoms of tetany, but steatorrhoea had apparently been present for the same time. It seems likely that hypocalcaemia insufficient to cause symptoms may have been present in the hypoparathyroid cases reported by Sutphin, Albright and McCune (1943) in which moniliasis appeared to precede other signs. The writer does not consider it justifiable to conclude, as these authors have done, that the fungus infection was responsible for the hypoparathyroidism.

Summary.

The dermatological changes associated with hypocalcaemia are considered in the light of the author's cases and others from the literature with particular reference to hypoparathyroidism. It is suggested that these are of three types.:

(1) Alopecia, transverse grooving of the nails, and oedema due to angiospasm and increased capillary permeability.

(2) Dry, scaly pigmented skin, scanty hair growth, and onychorrhexis due to prolonged calcium deficiency blocking enzymatic processes and interfering with the integrity of cell membranes.

(3) Secondary mycotic infection of the nails.

The possibility of a specific skin lesion in idiopathic hypoparathyroidism, and the problem of impetigo herpetiformis of Hebra are discussed.

It is a pleasure to thank the physicians and surgeons of the Western Infirmary for permission to report their cases. The biochemical investigations were made by Dr. S. V. Telfer and Mr. S. L. Rae, and fungus cultures by Dr. J. F. F. Smith. I am most grateful to Dr. J. Sommerville and Mr. J. M. McCorquodale of the Department of Dermatology for the photographs, and to Professor Sir John McNee for his advice.

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ON ELASTASE AND THE ELASTIC DYSTROPHIES OF THE SKIN.

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In 1890 Ewald published an important paper on the enzymatic dissolution of elastic fibres by extracts of pancreas. The active crude extract which he used was called "trypsin," but now that pure trypsin is obtainable, it has become doubtful whether trypsin is really responsible for elastolysis (Lansing, 1951). Realizing that elastolytic activity and pure tryptic action differed in many respects, Baló and Banga (1949*b*) gave the elastolytic factor a distinctive name, *elastase*. Although this factor can be concentrated, it has not yet been purified or identified as a single enzyme (Baló and Banga, 1950). Its chief action is to make highly insoluble elastin pass into solution. Since this is accomplished without the liberation of peptides or amino-acids, elastase cannot be proteolytic. There is some evidence that elastase can act as a mucinase (Hall, Reed and Tunbridge, 1952), but this may not be its only action.

The present study is an attempt to elucidate some aspects of elastolytic action and to apply it in the study of the elastic dystrophies of the skin.

Techniques Employed.

Elastin staining was done by Weigert's (1898) ferriresorcin-fuchsin method.

Elastin powder was prepared from the ligamentum nuchae of a bovine by extraction in boiling 0·1 N sodium hydroxide according to the method of Lowry, Gilligan and Katersky (1941). No fat solvents were used, since these are employed only when collagen is to be estimated in the same sample of tissue. Hall, Reed and Tunbridge (1952) claim that elastin so extracted contains no sulphuric acid which would otherwise interfere with the pH values of weakly buffered solutions.

Elastolytic activity was procured from dried, defatted bovine pancreas powder, freshly prepared by Willstätter and Waldschmidt-Leitz's (1923) method. A $2\frac{1}{2}\%$ concentration of the powder, well shaken in distilled water, was always freshly made before each experiment, centrifuged, and the supernatant fluid used for its elastolytic action. The solution was not further concentrated by any salting-out procedure.

Hyaluronidase digestion of sections was carried out with 1 mg. Hyalase (Benger) per ml. phosphate buffer of pH 6 for 3 hours at 37° C.

Buffers used were the Sørensen M/15 phosphate and 0·1 M glycine-sodium chloride-sodium hydroxide mixtures.

Toluol was used throughout as a bacteriostatic.

Test-tube experiments with beef elastin similar to those of Baló and Banga (1950) were performed for studying elastolysis. Tubes containing 20 mg. elastin, 1 ml. buffer and 0·3 ml. aqueous pancreas extract (elastase) with distilled water to 3 ml. were incubated at 37° C. for three hours as a rule. The amount of elastin dissolved was taken as the weight loss calculated from the dry residue of undigested elastin minus the weight loss of the residue in the control tube without enzyme.

Elastase digestion of sections was done using the same proportions of solutions as in the test-tube experiments, the buffer being between pH 10·5 and 11. Before hydration, the formalin-fixed paraffin sections were painted with 1% celloidin across one half only. After drying and hardening, the celloidin protected the covered half of the section from the enzyme and assisted in anchoring the uncovered half despite the loosening effect of the alkaline buffer and the enzyme. After digestion for $\frac{1}{2}$ to 3 hours the whole section was covered with celloidin and stained. By this means the half of the section covered initially acted as a simultaneous control.

Periodic acid-Schiff (PAS) reactions on sections were tested by McManus's method. Blocking of the reaction was carried out with acetic anhydride alone and with a mixture of acetic anhydride (40%) and pyridine (60%) by the method of McManus and Cason (1950).

Aldehyde reactions and aldehyde blocking reactions on sections followed the methods suggested by Danielli (1953). They were performed on formalin-fixed paraffin-embedded tissues dehydrated with alcohol.

Mallory's phosphotungstic acid-haematoxylin stain was used on the sections with preliminary mordanting in $2\frac{1}{2}$% iron alum for an hour.

Fractional Components of Elastic Fibres.

(a) *Protein-polysaccharide-sulphuric acid fractions.*—The protein elastin is probably extracted in greatest purity from tissue that is boiled in decinormal sodium hydroxide. It is recovered as the undissolved residue, and its dissolution by elastase is then the most rapid in comparison with the digestion of extracts otherwise prepared (Baló, Banga and Nowotny, 1949). When other methods of extraction are used (acetic acid, urea) it appears that the elastin in certain tissues may be less adequately isolated, and other substances may cling to it which retard its enzymatic digestion. These are presumed also to be constituents of the raw elastic fibre. They include a protein which, when freed from elastin, causes polysaccharide and sulphuric acid to be released. This whole complex has been called *elastomucin* by Hall *et al.*, and it may conceivably be related to the mucinous substance which appears in the site of elastic degeneration in blood vessels (Baló and Banga, 1949*b*).

Experimental.—Using the test-tube technique the curve of pH against elastolytic activity was plotted. The results (Fig. 1) resemble those of Baló and Banga (1950), although these authors studied only the initial velocity of the enzyme reaction. This curve decided the choice of a pH between 10·5 and 11 for the digestion of sections.

(b) *Lipoid fractions.* –There is evidence that fats play some part both in natural elastic degeneration and in the enzymatic dissolution of elastic tissue. Elastin presumed to be fat-free still yields a small lipoid fraction, chiefly

sphingolipid, when acted upon by elastase (Lansing, 1951). The influence of fat solvents on elastolysis is also relevant here, because they are used in preparing paraffin sections, and are actually recommended as a preliminary to enzyme action (Romeis, 1948).

Experimental.—Test-tube experiments were conducted using elastin powder prepared without the aid of fat solvents. The elastin in four tubes was treated for 24 hours with a fat solvent, which was then removed. After three hours' action of elastase at pH 10·5 the following percentages of elastin were left

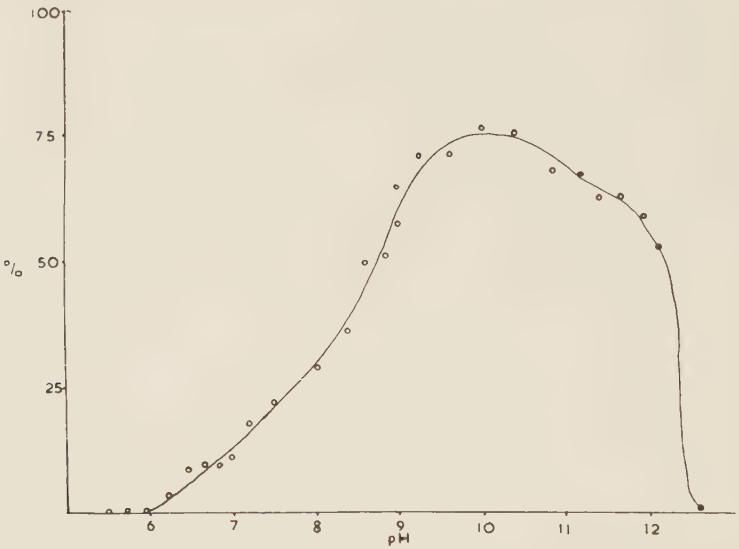


Fig. 1.—Digestion of elastin from ligamentum nuchae by elastase. Curve showing the influence of pH of the buffer solution on percentage of elastin digested in 3 hours at 37° C.

undigested in the tubes : control, 25% ; hot ether, 32% ; cold acetone, 35% ; hot acetone, 45% ; hot chloroform-methanol, 66%. It is clear that the fat solvents used retard the action of elastase. Purposely to de-fat sections before digestion seems inadvisable, as this appears to toughen the elastin.

Inhibition of Elastase Activity by Weigert's Elastic Stain.

Baló and Banga (1949) observed that an elastic fibre stained with Weigert's stain could not be digested and conversely a digested fibre failed to stain. Some observations were therefore made on this antagonism. Attention was paid to fixation and staining, and the effect of de-fatting with petrol-ether and treatment of the sections with hyaluronidase on the subsequent digestibility of elastic fibres.

Experimental.—Paraffin sections from lymphoedematous skin rich in elastic

fibres were used. It was first confirmed that Weigert staining inhibited elastolysis, and it was also shown that an initial three-day immersion of sections in petrol-ether retarded elastolysis. The enzyme fluid was found to remove the slight tinting which the ground substance shows with Weigert's stain.

The influence of the ground substance on the inhibiting action of Weigert's stain was first investigated. Sections were treated with hyaluronidase (H), Weigert's stain (W) and elastase (E) in the following sequences: HEW, HWE and WHE. These tests showed that Weigert's stain inhibited subsequent elastase action irrespective of the use of hyaluronidase before or after staining. It was also noted that hyaluronidase treatment revealed many smaller elastic fibres which usually remain obscured by the ground substance.

Weigert's staining solution was then examined for possible factors causing elastase inhibition. A " blank " stain was prepared, such as was first studied by Fischer (1902), containing all the ingredients except the dyestuff itself basic fuchsin—but otherwise made in the same way. Immersion of sections in this fluid for the usual staining time of one hour was found not to inhibit the subsequent action of elastase. It was therefore concluded that it was the actual staining which was responsible for the inhibition of elastolysis in tissue sections.

Test-tube studies were undertaken to investigate the same problem on powdered elastin. Tests were made on elastin alone (E), after formalin fixation (F), stained with Weigert (W) and de-fatted in hot chloroform-methanol (D) in the following combinations: E, EF, EFW, ED and EDW. Formalin fixation did not retard subsequent digestion but de-fatting again retarded it. Weigert staining did nothing further to retard, and may even have enhanced, subsequent enzyme action. Powdered elastin thus behaved very differently from the elastic fibres in sections. This suggests that the native fibre contains reacting substances other than elastin which prevent enzyme attack after staining.

Elastin powder stained violet with Weigert's stain as did the elastic fibres in sections. On digestion of such stained powder, the supernatant fluid became a violet colour as the elastin passed into solution. The lipoid fraction separated out unstained. Attempts to dialyse the violet dye in the supernatant fluid through collodion tubes were unsuccessful, suggesting that the dyestuff was still bound to the elastin molecules and that this was responsible for its being held back by the membrane.

Action of Elastase on the Elastic Dystrophies of the Skin.

Although the elasticity of the skin is altered in several other conditions, it is only in the three diseases studied here—pseudoxanthoma elasticum,

senile elastosis and colloid milium—that a primary dystrophy of the elastic fibres is considered important.

(a) *Pseudoxanthoma elasticum.*—Most authors have agreed with Darier that pseudoxanthoma elasticum is a dystrophic disease of elastic tissue (Gans, 1925 ; Freudenthal, 1932 ; Pautrier and Woringer, 1938). However, Hannay (1951) has suggested that in this condition there is too much elastic-staining material, degenerated or otherwise, for all of it to be actual elastic tissue, and that it could have another origin, being perhaps derived from collagen. The facts that the fibres branch and can become encrusted with lime were for some reason regarded as additional evidence against their being elastic fibres. Further, the electron microscope revealed no recognizable elastic in the skin of his cases. These were evidently the main grounds for deriving the degenerated substance from a source other than the elastic. In the studies outlined below the classical view on the pathogenesis of pseudoxanthoma elasticum received support.

Experimental.—Sections from a typical case of pseudoxanthoma elasticum were treated with elastase (Fig. 2). The elastic tissue around the pathological

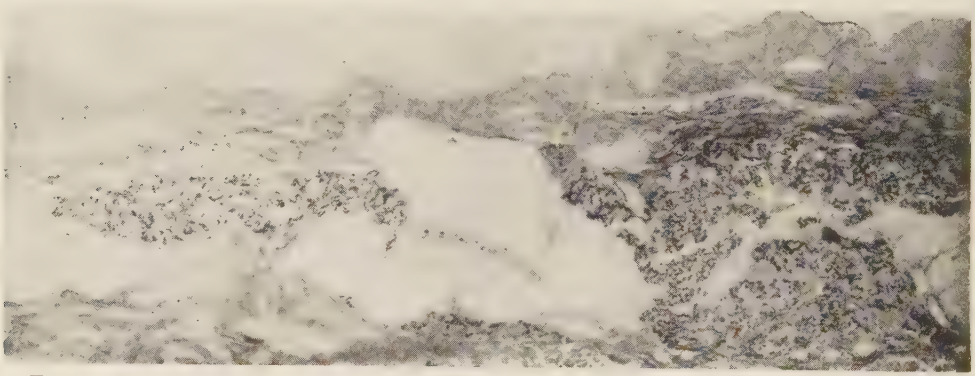


Fig. 2.—Pseudoxanthoma elasticum. Section of skin in which the left half of the preparation is partially digested with elastase, while the right half acts as a control, being previously coated with celloidin. On the right a zone of normal elastic is seen under the epidermis beneath which a pseudoxanthomatous area is found containing abnormal elastic tissue. On the left the corium is seen to have lost its normal elastic fibres. An island of pathological elastic fibres still persists, though these fibres are sparser and less well stained than in the control half. The sebaceous glands appear as large unstained spaces. Weigert's elastin stain.

nodules was uniformly dissolved. The degenerated masses within the nodules were also dissolved, but showed a slightly greater resistance to solution than the surrounding normal fibres. They exhibited further all the changes attendant upon normal elastolysis—general reduction in intensity of staining, segmentation and ballooning of fibres, erosion, flocculation, granular and fibrillar degeneration. Some of the elastic conglomerates were PAS-positive. Collagen withstood the action of elastase.

(b) *Senile elastosis.*—In a recent note, Lansing *et al.* (1953) state that in senile elastosis the abnormal tinctorial reactions seen are not due to collagen, that the altered elastic tissue is susceptible to elastase digestion, and that the pathological tissue is recognizable as elastic under the electron microscope.

In the present investigation of senile elastosis there were considered to be three stages of elastic degeneration which could be traced through transitions from the normal elastic. Proceeding towards the skin surface from below, there is first the well-known change of elastin to elacin. Next, there is a lessening of Weigert-positivity, and the elacin fibres show " islands " of PAS-positivity along their course. Nearer the surface, the masses of PAS-positive material unite to form the colloid of senile elastosis. This last change has sometimes been called collacin formation, but Mallory's phosphotungstic acid-haematoxylin allows one still to see the fibre elements and to distinguish the orange-staining elastic contribution from the slight, irregular and pale red-staining contribution from collagen.

Experimental.—Elastase promptly removed the areas of colloid change and incipient colloid change, abolishing their slight staining reaction with Weigert and their strongly positive reaction to PAS. Less promptly dissolved were the normal elastic fibres, some of which became PAS-positive during the process. Elacin remained intact the longest, but was nevertheless easily digested.

Some histochemical studies were undertaken to investigate the nature of the PAS-positive material on the sections. The techniques used were : periodic acid oxidation (PA), for converting 1,2 glycol groups of sugars to aldehydes ; Schiff's reagent (S) for aldehydes ; 2,4 dinitrophenylhydrazine in normal hydrochloric acid solution (DNPH) for aldehydes and blocking of aldehyde groups ; acetic anhydride (AA) and pyridine (Pyr) for acetylation of glycol groups and blocking of PA ; mercuric chloride solution ($HgCl_2$) for hydrolysing the acetal linkage in lipid aldehydes ; chloroform-methanol mixture (Ch/Me) for 24 hours at 37° C. for removal of lipoids. The following sequences were tried : S ; PA.S ; AA.PA.S ; AA-Pyr.PA.S ; Ch/Me.PA.S.; $HgCl_2$.S ; DNPH.PA.S ; PA.DNPH.PA.S. It was found that the material giving the PAS-positive reaction in the elastic of senile elastosis was not removed by lipoid solvents, failed to show the presence of the acetal linkage of lipid aldehydes, and did not contain free aldehyde. When acetylated with acetic anhydride : pyridine (40 : 60) its PAS-positivity was completely lost, and partially so when acetic anhydride alone was used. From this it may be deduced that carbohydrate alone without lipoid is responsible for the positive PAS-reaction in senile elastosis.

(c) *Colloid milium.*—Ferreira-Marques and van Uden (1950) have reviewed the pathogenesis of colloid milium, and conclude that the colloid substance comes from degenerated elastic tissue.

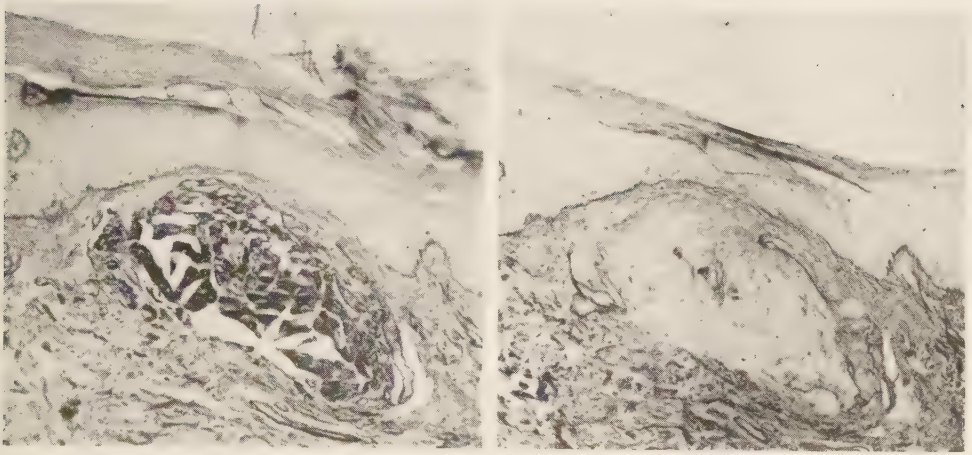
In sections from a typical case this derivation could be confirmed. Using Mallory's phosphotungstic acid-haematoxylin, it can be seen (Fig. 3) that the altered elastic fibres in a zone of active colloid formation stain blue-black and show the following transformations: the fibre becomes swollen and stains an orange colour, while the blue-staining material disperses as a fibrillar and granular residue on the orange background. The orange material then swells further, losing both its fibrous form and the blue granular residue.

FIG. 3.—Colloid milium. Section from the active edge of a milium showing how pale and dark components of the elastic fibres become manifest, the pale portion forming the colloid. On the left is a mass of irregularly swollen darkly staining fibres. Towards the right the dark material is progressively lost, although it persists in shreds on the fibre. The light-coloured fibre relic swells, fuses with similar material from other fibres, and thus forms "colloid." A mass of colloid so formed is seen in the right upper quadrant of the photograph. Mallory's phosphotungstic acid-haematoxylin; oil immersion.

It then fuses with similar masses to form the actual colloid milium. Swollen elastic fibres and their colloid end products were found to take the PAS-stain strongly (Fig. 4*a*). A collagenous contribution to the colloid, if any, could not be determined from the material available.

Experimental. Elastase digestion of sections of colloid milium showed prompt removal of colloid with consequent loss of PAS-positivity (Figs. 4*a* and *b*). The normal elastic fibres withstood removal longer.

It was further established that hyaluronidase was without effect on the colloid material. Exposing the colloid merely to the alkaline buffer used during elastolysis also failed to remove it.



(*a*) (*b*)

FIG. 4.—Colloid milium. (*a*) Strongly Schiff-positive milium of typical histological structure. (*b*) Section through another part of the same milium, after digestion with elastase, followed by periodic acid-Schiff staining. Removal of all Schiff-positive material in the milium by elastase. Periodic acid-Schiff; low power.

The positive PAS reaction could be completely blocked by preliminary acetylation with the acetic anhydride-pyridine mixture. Presumably therefore the reaction is attributable to the presence of a carbohydrate and not a lipoid.

CONCLUSIONS.

When normal or abnormal elastic is digested by elastase in tissue sections, fibres which are morphologically identical show a variable susceptibility to the enzyme. In spite of this, certain general trends can be established.

Certain changes are associated with an *increased resistance* of elastic fibres towards elastase. In degenerative diseases the fibre toughens. This is seen in the elastorrhexis and elastoclasis of pseudoxanthoma elasticum and also in the elacin of senile elastosis. A comparable toughening can be produced artificially by fat solvents and chemical procedures which cause "denaturation" (Baló and Banga, 1949*b*). Such fibres then stain with many dyes which are not normally selective for elastic tissue.

Complete inhibition of the enzyme action on sections is produced by Weigert staining. This phenomenon depends on some property of the elastic fibre other than its pure elastin content. It is caused by the actual dyeing process, and is independent of any mordanting action of the stain solution. However, elastin itself is responsible for the purple colour of the stained fibre. It may be mentioned also that an elastase inhibitor is present in the blood serum of normal subjects. This was noted by Baló and Banga (1949*a*), and has been confirmed by Erasmus working in this department.

Facilitation of elastolysis seems to depend on an initial separation of an elastomucin from the fibre. In disease this is seen when the elastic fibre and its colloid products of degeneration take up the PAS stain. Colloid change in senile elastosis and the colloid of colloid milium react similarly in this respect. The evidence also suggests that normal fibres may pass through a PAS-positive phase during elastase digestion. Release of a carbohydrate component is probably responsible for this PAS reaction. Lipids, and lipid aldehydes particularly, are not involved.

In pseudoxanthoma elasticum, senile elastosis and colloid milium, the behaviour of sections of skin towards elastase suggests that they are in fact elastic dystrophies, and the alteration of the elastic fibres is in conformity with present conceptions of the chemistry of the elastic fibre. The morphological peculiarities of the elastic dystrophies have not as yet been elucidated by knowledge of the fibre chemistry.

Summary.

In the primary degenerative diseases of elastic tissue of the skin, the fibres may pass through a stage in which they show a raised resistance towards elastase and stain non-specifically. Thereafter a colloid degeneration of elastic may be seen in which a carbohydrate-containing substance is liberated, readily removable with elastase but not with hyaluronidase. So-called pure elastin as isolated chemically shows some different reactions. These probably arise from the removal of other components which are present in the intact elastic fibre.

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ACNEIFORM ERUPTIONS IN INFANCY.

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Acne in infants is not as uncommon as one might conclude from most text-books. Although Giknis and his colleagues in 1952 could find only 24 cases recorded in the literature, to which they added another, I have records of ten patients, in five of whom the lesions appeared within the first two months of life. "Grouped comedones" in infants and children were first described by Radcliffe-Crocker in 1884; his three cases showed lesions on the face, but other authors such as MacLeod (1905) have reported grouped comedones on the trunk and other areas which had been rubbed with camphorated or other oils. I believe that this latter type is a separate entity and I shall not deal with it, but will limit myself to lesions occurring on the face unrelated to any inunction of oil. Children with this latter type may be roughly divided into two groups: those in whom the spots appear in the first few weeks of life —the true acne neonatorum—and those in whom they occur at about a year old or more (see Table I). This distinction, however, is not always easy as the history is often rather vague, and as Giknis *et al.* point out, the more detailed the report of a case the younger the age of onset appears to be. Nevertheless, in my older group I do not think the mothers would have disregarded the spots for as long as a year and probably the later age of onset is correct. In most recorded instances typical lesions were noted by three months; in at least four out of five cases of mine they were present in the first fortnight of life; the fifth child was adopted and his history before two months was not known.

In those cases which were followed until remission occurred the duration was usually less than 8 months, pitted scars being the only residue (Giknis *et al.*). This is not my experience, for out of five cases starting in infancy two cleared quickly, but the others were active at 14 months, 21 months and 5 years respectively. In three of the older group two cleared quickly and one by 18 months. My impression is that in the latter type the lesions tend to be fewer, sometimes even solitary, and may take the form of a cold abscess.

One other striking feature is the preponderance of males over females. Giknis *et al.* found 13 boys against 5 girls. In my younger series all five patients were boys, though in the older group there were three girls and two boys.

There has been considerable discussion as to whether acne neonatorum is of the same nature as acne vulgaris, or whether it is a reaction to some external

TABLE I.

	Sex.	Age when seen.	Stated age of onset.	Family history.	Type.	Age when last seen.	
J. D—	F.	18 months	12 months	—	Cold abscess on right cheek	..	..
D. A—	M.	15 „	12 „	—	Tiny papules on forehead and sides of face	..	..
M. P—	F.	18 „	15 „	None	Small acneiform lesions over cheeks with a number of cold abscess lesions	9 years	Cleared quickly. A little pitted scar on each cheek.
S. W—	F.	14 „	9 „	„	Grouped comedones over both cheeks	7 „	Cleared by about 18 months
K. G—	M.	7 „	? 4 „	—	On face	14 „	A little scarring on left cheek.
J. A. C—	M.	8 „	2 „	Not known	Papules and some pustules over cheeks and chin. Typical acne	14 months	Still some comedones.
I. J—	M.	9 „	At birth	Father had acne	Comedones over cheeks. Occasional infected indurated lesions	9 years	Cleared fairly quickly. Residual pitted scar on each cheek.
G. S—	M.	8 „	Traces at birth; marked at 2 weeks	Father had severe acne	Numerous comedones over cheeks with pustules on left side	10 months	Practically clear with one month's treatment.
P. Y—	M.	7 „	10 days	Uncle had acne	Comedones on cheeks and chin with a few small pustules	14 years	Comedones still present at 21 months. Relapsed at 11 yrs.; bad at 14 yrs.
M. L—	M.	3 years	2 weeks	None	Comedones on face with pitted and somewhat keloidal scarring in centre of cheeks	5 „	Still present at age 11; attending Birmingham Skin Hospital.

factor such as oil or grease or, in a breast-fed baby, contact with milk. The occurrence of the condition in bottle-fed babies and the absence of any history of applications to the skin make the latter explanation unlikely in many cases. Radcliffe-Crocker thought grouped comedones were due to warmth and moisture and perhaps other irritants in predisposed subjects ; he attributed the spots in infants to the child being held closely to the mother in nursing. The following case, which I believe to be unique in the literature, provides convincing evidence that acne neonatorum and acne vulgaris are essentially the same condition.

P. Y—, a boy, started with spots on the cheeks at 16 days old ; when seen at 7 months he showed comedones on the cheeks and chin with a few small pustules (Fig. 1). These were still present at 21 months but cleared later. The spots relapsed at 11 and by 14 he showed typical severe acne (Fig. 2).

Further suggestive evidence is the fact that in two out of four of my younger series the father had acne and in a third an uncle was affected.

From the above I suggest that in these children we are dealing with an acne-prone subject who under some specific stimulus produces comedones, first in infancy and later in adolescence, but that the fundamental process is the same at both ages. If we can assume that acne in infants is essentially the same as that in adolescents we are faced with the problem of how the acne is produced. Ordinary acne is supposed to be due to an increase in the androgen/oestrogen ratio or possibly, according to Haskin *et al.* (1953), in the progesterone/oestrogen ratio in women. Androgens are produced by the adrenal cortex and the testes, the former being much more important in childhood. That these can provoke acne in children was shown by a child of 8 months reported by Talbot *et al.* (1952) with an adreno-cortical carcinoma who had facial acne ; but he also showed hirsutism, enlargement of the genitalia, and other signs of masculinization. In congenital bilateral hyperplasia of the adrenal cortex acne usually develops before the fifth year, but here also are other abnormalities such as accelerated growth and development of sex hair. In the children here described there was no evidence of any masculinizing change.

In normal children the amount of androgens produced as estimated by the 17-ketosteroids in the urine is minimal, being less than 1 mg. per day up to the age of 8 ; it seems unlikely that this could be sufficient to produce acne even if there were a relative increase in the androgens compared with the oestrogens. Hamilton (1941) maintains that whatever the androgen/oestrogen ratio, a certain threshold amount of androgens must be present before acne appears. It is just possible that steroids other than those excreted as 17-ketosteroids may play a part in the production of comedones, in which case estimation of the latter would give a false impression of the comedone-producing activity of the adrenals. However, acne does not occur in eunuchs in whom

FIG. 1.

FIG. 2.

adrenal function is normal. It seems unlikely therefore that adrenal androgens produced by an otherwise normal infant can account for the acne.

An alternative explanation is that the child may be influenced by maternal hormones. That this can occur is shown by the frequent occurrence of pseudo-precocity in the newborn. The majority of female infants, according to Talbot *et al.*, show transient sexual precocity with hypertrophy of the labia and thickening of the vaginal epithelium, which contains glycogen for 3 or 4 weeks. Slight vaginal bleeding occurs in 1% and the breasts frequently enlarge and secrete "witches milk." By the end of the 4th month the breasts have reverted to the infantile type. These are, of course, oestrogen effects and the oestrogen content of the child's blood corresponds to that in the mothers. There is, however, also an increase of progesterone in the maternal blood in the latter part of pregnancy (Wilkins, 1950). Haskin *et al.* have shown that in the rat the administration of progesterone produces an increase in sebaceous gland size comparable with that induced by testosterone, so that it is reasonable to assume that the high content of progesterone in the maternal blood would have the same effect in the infant.

Hamilton has shown that in eunuchs treated with testosterone only a proportion develop acne presumably only those whose constitutional tendency predisposes them to acne when adequately stimulated. The infrequency of acne in infants may be similarly explained, only those infants with a high degree of susceptibility being provoked to produce comedones. Alternatively, or possibly additionally, there may be some mothers who develop a particularly high content of progesterone in the blood towards the end of pregnancy. This would account for acne neonatorum, but it is unlikely that the direct effect of the maternal progesterone could last more than a few weeks ; any oestrogen effect at any rate disappears by the fourth month. Hamilton found that acne produced in eunuchs by testerone was markedly diminished a week after the injections were stopped and had practically disappeared in 6 weeks. It is possible that other influences such as infection, friction, etc., may keep going an acneiform process which has been initiated by maternal progesterones. Such a mechanism could not explain those cases which develop after 12 months or more. For these one can only surmise that they are caused by other provoking factors such as infection or external irritation, or conceivably that the child has such a strong acne tendency that its skin reacts to even minimal traces of androgens.

These observations suggest the following conclusions :

(1) That acne neonatorum is essentially the same condition as acne vulgaris.

(2) That it occurs only in constitutionally predisposed children who are likely to develop ordinary acne vulgaris in adolescence.

(3) That acne developing in the first few weeks of life may be due to the influence of maternal progesterone.

Summary.

A patient with acne neonatorum is described who later developed severe adolescent acne. The mechanism of the condition is discussed.

I would like to thank Dr. Ingram for allowing me to refer to some of his patients.

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THE PROCEEDINGS OF THE TENTH INTERNATIONAL CONGRESS OF DERMATOLOGY

A limited number of copies of the Proceedings are available at the price of £3 3s.

Particulars may be obtained from the Editorial Secretary, St. John's Hospital for Diseases of the Skin, Lisle Street, London, W.C.2.

NORTH BRITISH DERMATOLOGICAL SOCIETY.

Dundee, 11 June 1953.

Primary Tuberculous Complex of the Skin.—Dr. O. A. Finn.

A boy, aged 16.

History.—He fell into a stream in July 1952 and abraded his right elbow. The wound at first seemed to heal but about ten days after the injury it unexpectedly broke down.

In September 1952, axillary adenitis with cold abscess developed.

He came to the skin department in January 1953, and was found to have a patch of lupus vulgaris on the right elbow and a sinus in the axilla.

Family history.—No family history of tuberculosis.

Investigations.—Skiagram of chest : Normal.

Mantoux 1 : 10,000 : Positive.

Histology.—Consistent with lupus vulgaris ; no acid fast bacilli seen.

Treatment and progress.—Isonicotinic acid hydrazide 300 mgm. daily, and streptomycin 1 g. daily produced healing of the axillary sinus and a marked improvement in the lupus vulgaris lesion.

Chronic Discoid Lupus Erythematosus treated with anti-malarial drugs. Dr. O. A. Finn.

Four cases (3 women and 1 man) were shown to illustrate 26 patients with chronic discoid lupus erythematosus who are being treated with chloroquin 0·25 g. daily (Avlocolor, I.C.I.). Of the 4 cases, 3 had been treated with mepacrine in 1952 (2 cleared ; 1 much improved), but had relapsed this year.

The results with chloroquin to date, viz., 8 completely cleared, 3 much improved, and 15 improved, are comparable with those obtained with mepacrine therapy, although it is too early to give a final assessment. Side effects (nausea, headache, giddiness) seen in a few cases have been slight. Chloroquin has the great advantage over mepacrine of not staining the skin.

Rodent Ulcer following Thorium X Therapy.—Dr. J. Rogers.

A boy, aged 10.

He was treated from June 1947 to February 1953 with thorium X varnish (3000 e.s.u. per c.c.) for a pale capillary angioma of the right side of the face. A total of 35 applications were given at intervals varying from two weeks to three months. In March 1953 a flesh-coloured nodule 8 mm. in diameter was noted in front of the right ear. Excision of this nodule revealed an undifferentiated basal-cell carcinoma.

Comment.—The early occurrence of this basal-cell carcinoma appears to be due to the prolonged treatment with thorium X.

The following cases also were shown :

Lipomelanic Reticulosis in an Infant ; Scleroderma ; Acne Necrotica.—Dr. J. Kinnear.

Trichoepithelioma. ? Subacute Lupus Erythematosus ; Leukaemia Cutis ; Pemphigus Vulgaris ; Leprosy.—Dr. J. Rogers.

Necrobiosis Lipoidica Diabeticorum ; Untoward Result of B.C.G. Vaccination.—Dr. O. A. Finn.

BOOK REVIEWS.

An Atlas of Dermatology.*

The first three parts of this atlas have already been reviewed (**65**. 105) and the fourth and fifth have now been published and in every way fulfil the promise of the earlier numbers.

The fourth number consists almost entirely of a beautiful collection of syphilitic lesions, and one wonders that the authors have still been able to find the variety of cases. Such is the reduction in clinical material in the United Kingdom that in years to come more and more reliance will be placed on an atlas such as this.

The fifth part contains Leiomyoma, Dermatitis Chronica Atrophicans, Dermatitis Striata Pratensis, Fox-Fordyce Disease, Radiodermatitis and more Syphilis.

As these numbers arrive the whole work seems at first rather patchy but it develops its form as fresh subjects are interleaved with the old ones. At present, for example, it seems strange that dermatitis striata pratensis should be given one plate and three pages of script, while the general subject of phytophotodermatitis is mentioned only in passing. Presumably, in a future number, the whole subject of light sensitivity will be dealt with in more detail. F. R. B.

Yaws Control.†

Parts I and II deal with the biology of Yaws and with antibiotics in its treatment. Most of the rest is concerned with various aspects of large scale control in various parts of the tropics and is of importance primarily to the public health worker and expert in tropical diseases.

Laboratory studies show that strains of syphilis, yaws and bejel treponemes show substantial degrees of cross-immunity in animals; the Treponema Immobilization Test promises to give further valuable information in this problem. Another important observation is that treponemes have not yet acquired penicillin resistance.

Under the title "Non-specific Factors in Yaws Epidemiology" Hill discusses many aspects of the problem. His remarks on immunity and cross-immunity with syphilis are a good summary of present day views.

The mass yaws-eradication campaign launched in Haiti in 1950 was used to test the efficacy of a single dose of 600,000 units of penicillin given as penicillin G with procaine in oil with 2% of aluminium monostearate; a satisfactory blood level is obtained for 72 hours. The results of this "therapia magna sterilisans" were excellent and include 100% clinical cure in cases of primary yaws and around 90% in secondary and "wet crab" cases. Equivalent results are obtained in syphilis only with 4 times the amount of penicillin used. The use of other antibiotics by mouth is also reported; terramycin gives results comparable with penicillin but has the disadvantage of requiring oral administration daily for two weeks.

The syphilologist will find much to interest him in the first two parts of the symposium: the remainder should be read by all, and not only medical men, who see the implications of a successful international alliance against a common unicellular enemy. L. J. A. L.

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* *Atlas de Dermatologie*. By P. de Graciansky and S. Boulle. Paris: Librairie Maloine S.A., 1952. 320 coloured plates. To be issued in 20 Parts. Price 2000 francs each. Obtainable from H. K. Lewis, London: Prospectus free on request.

† *First International Symposium on Yaws Control, Bangkok*, 1952. World Health Organisation: Monograph Series, No. 15. Pp. iv + 418. 32 plates. Price 22*s*. 6*d*.

Classics in Dermatology.*

If proof were needed that dermatology has come of age, these historical pages provide it. It cannot be disputed that the story begins with Robert Willan (1798), as is here maintained. He is our acknowledged founder, in that he was the first to conceive a classification based on "the morphology of the essential lesion." Succeeding dermatologists the world over adopted his principles, which have persisted with only minor modifications through a century and a half to the present day.

Willan was very fortunate in his choice of an assistant and subsequent biographer, a fellow Yorkshireman, Thomas Bateman, who deservedly followed his master in the little Public Dispensary in Cary Street in 1811. His name too is enshrined in our annals as the author of a "masterful and most influential *Synopsis of Cutaneous Diseases*" (1813) and the first *Atlas of Dermatology* (1814-17).

About the same time Jean Louis Alibert, the great French pioneer, was appointed dermatologist to the recently built St. Louis Hospital, from that day onwards the abiding centre of dermatology in France. He propounded the so-called Linnean classification of cutaneous diseases. It was found impracticable and was soon abandoned in favour of Willan's conception. Nevertheless, as the St. Louis wards testify, Alibert came to be regarded as the father of dermatology in France. He was moreover a brilliant physician and clinical teacher.

Less-known names than his follow in this Part I, "Early Workers." They are not all those of dermatologists. Among them is Armand Trousseau, the famous French physician and teacher, the first to recognize diphtheria of the skin. More to the point are discussed the writings of Ernest Bazin, Camille Gibert, Alphée Cazenave, the discoverer of pemphigus foliaceus and lupus erythematosus (1851), and Alphonse Devergie—all outstanding dermatologists of the earlier period.

Ferdinand von Hebra rightly heads the list in Part II—"The Middle Period." He was undoubtedly the greatest dermatologist of his time; his clinic became the Mecca and shifted the centre of teaching from England and France to Austria for about 40 years (1841–80). Hardly less eminent was his successor and son-in-law Moritz Kaposi, who, like Hebra, gave his name to more than one dermatological entity.

The torch now flared up again in Great Britain. Yet a third Yorkshireman—Jonathan Hutchinson—closely followed by Radcliffe-Crocker and Colcott Fox added further lustre to our achievements, while in America our knowledge was enriched by Louis Duhring, J. A. Fordyce and J. C. White, who was the first dermatologist to be allotted a professorial chair in the U.S.A., and the inventor of that most valuable adjunct to therapy, the CO_2 freezing pencil. In France too this "Golden Age" (Part III) was maintained by E. Besnier, E. Vidal, Henri Hallopeau, B. R. Schenck and A. Poncet. Norway produced Caesar Boeck and Italy, Domenico Majocchi.

Part IV concludes the series with a long list under the heading "More Recent Observations." Outstanding among these contributors are J. L. Brocq, E. Ehlers, J. Jadassohn, E. Jacobi, J. F. Schamberg, J. T. Bowen, R. L. Sutton, J. Darier, F. Parkes Weber, Bruno Bloch, Erich Urbach, M. B. Sulzberger, Gustav Riehl, Aldo Castellani, H. Gougerot, C. Guy Lane—an epoch at least as brilliant as that labelled the "Golden Age."

There are 107 illustrations in the text. Of these 56 are portraits of the majority of the 95 chosen contributors. They are of great value and interest, both historically and to the student of character. The remaining 51 are reproductions of original plates of clinical cases. Many of the earlier examples are very crude, quite valueless

* *Classics in Clinical Dermatology, with Biographical Sketches.* By Walter B. Shelley and John T. Crissey. Springfield, Illinois: Charles C. Thomas, 1953. Oxford: The Blackwell Scientific Publications. Pp. 467. 107 illustrations. Price 75*s.* 6*d.*

as diagnostic aids, and might well have been omitted. The basic arrangement of the extensive material is chronological—obviously the best that could have been devised —and there is an excellent index.

As was anticipated in the preface there are inevitable omissions, some of them rather glaring. The French School will deplore the non-inclusion of Sabouraud and Pautrier, the German, that of Lassar, Arning, E. Hoffmann and Arzt, while we in this country could have suggested British names as least as worthy of consideration as some of the non-dermatologists selected by the authors. But such criticisms are inevitable in any compilation of this kind. They could and should be met in a subsequent edition of the work, which will be rendered necessary at some future date, if the fraternity acclaims it as it deserves.

Drs. Shelley and Crissey have worthily achieved what they set out to do, and as Professor J. H. Stokes remarks in his introduction, "These vignettes of the masters in action in the past are more than timely and a spur to an even more distinguished future." H. C. S.

Semon's Atlas.*

The bedside is the best place to learn clinical medicine and a knowledge of skin diseases must be based on the clinical examination of patients. Many dermatoses are diagnosed on appearance alone, and in dermatology gaps in the physician's clinical experience can be filled by good illustrations : thus a good atlas of skin disease is very necessary in the library of a well-equipped clinician. Several times I have had patients referred to me correctly diagnosed by the practitioner because, as they say in their letter, the eruption looks like the picture in Semon's *Atlas*. The publication of a fourth edition in less than 20 years is conclusive proof of the demand for this book, and the new edition can be thoroughly recommended.

Photographs of living patients are always better than pictures of moulages, and with very few exceptions these colour illustrations are excellent. The exceptions are Plate 54 (granuloma annulare), and Plate 113 (tinea circinata), neither of which would help a non-dermatologist to diagnose these conditions. In addition, the colour of Plate 64 (acute lichen planus) is not characteristic of this condition in the eruptive phase which is the time when the practitioner most needs help. I mention these to stress the excellence of the remaining 144.

However, the great value of this book is in the discussion of the diseases illustrated. Here one has the views of a mature experienced acute observer expressed in beautiful language ; the chapters on the common conditions impetigo, lupus erythematosus, lupus vulgaris and pityriasis rosea are particularly good and have obviously been written against the background of numerous patients closely observed. There are wise words about the conduct of a medical witness in court and to the questions, "Is it syphilis ? is it scabies ?" when confronted with an unusual rash, I would add "Is it a drug ?"

The methods of treatment recommended are those which the author has found to work. Therapy is as up to date as possible, and where several methods are mentioned he discusses the advantages and disadvantages of each. The only error I detected in the text was on page 152, where the ophthalmic nerve is given as the middle division of the fifth cranial nerve, but again this small error emphasises the excellence of the whole.

The binding, paper and colour photographs are of a high standard and the index is full. This book can be thoroughly recommended to the general practitioner and student for help in recognizing the common dermatoses, and to the dermatologist for the delightful demonstration of Dr. Semon's wisdom. H. R. V.

* *An Atlas of the Commoner Skin Diseases.* By Henry G. C. Semon and Arnold Moritz. 4th edition. Bristol : John Wright & Sons, Ltd. Pp. 379. 147 colour plates. Price 75*s*.

CURRENT LITERATURE

SENSITIVITY TO COMPOUND G–4 ("DICHLOROPHENE") IN DENTIFRICES. A. A. Fisher and L. Tobin. (1953) *J. Amer. med. Ass.*, **151**, 998.

Compound G–4 ("Dichlorophene"), a potent fungicide and bactericide, has been incorporated in certain toothpastes and toilet preparations. Nine patients who developed a syndrome consisting in varying degrees of stomatitis, glossitis, cheilitis, perleche or circumoral dermatitis gave positive patch tests to G–4, which was in the toothpaste they had been using. Contact dermatitis of the palm caused by G–4 in toothpastes has also been reported. A. J. R.

SKIN TESTS IN ATOPIC DISEASE. J. M. Sheldon, K. P. Mathews and R. G. Lovell. (1953) *J. Amer. med. Ass.*, **151**, 785.

The authors consider that skin tests are a valuable laboratory procedure in allergic diseases if they are properly interpreted in the light of the clinical history. Cutaneous and intracutaneous tests for common inhalant allergens are said to be highly reliable, whilst skin tests for food hypersensitivity are often of doubtful value. A. J. R.

HYDROCORTISONE (COMPOUND F) ACETATE OINTMENT IN DERMATOLOGICAL THERAPY. M. B. Sulzberger, V. H. Witten and C. C. Smith. (1953) *J. Amer. med. Ass.*, **151**, 468.

The topical application of hydrocortisone acetate 1% to 5% in various bases was used on 62 patients with selected dermatoses. The ointment was definitely valuable in atopic dermatitis and of some value in anogenital pruritus. Several cases of lichen simplex and nummular eczema also showed some improvement. The ointment was of no value in chronic discoid lupus erythematosus, psoriasis, pemphigus vulgaris and alopecia areata. When there was a favourable response improvement occurred within 2 to 7 days, and beneficial effects usually wore off within 4 to 5 days after stopping the ointment. A. J. R.

OXYTETRACYCLINE IN THE TREATMENT OF OROCERVICAL FACIAL ACTINOMYCOSIS. S. L. Lane, A. H. Kutscher and R. Chavers. (1953) *J. Amer. med. Ass.*, **151**, 986.

Oxytetracycline hydrochloride (Terramycin) in a dosage of 750 mg. to 2000 mg. daily for 2 to 6 weeks was successful in 7 cases of orocervical facial actinomycosis. Six of them remained cured when followed up after an interval of 6 to 18 months. The remaining one had a recurrence within 3 months of finishing treatment. His original course had, however, been a small one, and after further treatment he was free from the disease when re-examined 3 months later.
A. J. R.

SURGICAL CORRECTION OF LYMPHOEDEMA. G. H. Pratt. (1953) *J. Amer. med. Ass.*, **151**, 888.

After discussing briefly the classification of the causes of chronic lymphoedema the author describes a new operative technique. The skin is removed to the thickness of 0·017 in. with the electric dermatome, all fascia and lymph components are radically excised and the patient's own skin is replaced on the muscle. In 25 such operations there has been no recurrence.
A. J. R.

TREATMENT OF DIFFUSE PROGRESSIVE SCLERODERMA. J. A. Evans, H. J. Rubitsky and A. W. Perry. (1953) *J. Amer. med. Ass.*, **151**, 891.

This is a long and valuable article based on the therapeutic experience at the Lahey Clinic with 38 patients with diffuse progressive scleroderma. A great many different procedures which have been advocated were employed in groups of cases or in individual cases. Para-aminobenzoic acid produced improvement in only 1 of 14 cases; 2 developed agranulocytosis. Diphenhydramine definitely improved 4 of 12 patients. Testosterone was ineffective in 5 cases but improved skin and oesophageal lesions in 2. Definite improvement occurred in 2 patients receiving antibiotics (Chloramphenicol and Terramycin). Neither cortisone nor corticotropin proved of benefit in 6 cases. Among other agents found ineffective were alpha-tocopherol, nicotinic acid, Priscol, ergosterol and "Bistrimate."

The greatest benefit was obtained from extensive sympathectomy, and moderate improvement

was recorded in 88% of 17 cases. Sympathectomy from the 1st to the 12th thoracic segments, leaving a gap on one side supplying the greater splanchnic nerve, is recommended as the oesophagus was involved in 65% of cases with facial involvement; a less extensive sympathectomy will not benefit oesophageal lesions. A. J. R.

"STILBAMIDINE" IN THE TREATMENT OF CUTANEOUS BLASTOMYCOSIS. J. C. Fink, D. E. VanderPloeg and M. P. Moursund. (1953) *J. Amer. med. Ass.*, **151**, 1395.

A patient with North American blastomycosis who had failed to respond satisfactorily to other forms of treatment was treated with Stilbamidine. The lesions involuted completely after a total dosage of 3·75 g. and there had been no recurrence three months later. A. J. R.

GENERALIZED DERMATITIS AND ACUTE LETHAL "SYPHILITIC" PNEUMONIA DUE TO AN ALLERGIC REACTION TO ARSPHENAMINE. H. N. Hadders and C. th. B. Wakkerman. (1952) *Acta derm.-venereol., Stockh.*, **32**, 288.

Simultaneously occurring anomalies in the skin and lungs after administration of certain drugs are considered to be allergic in nature. This view is backed up by the autopsy and microscopical examination of a 23-year old woman suffering from secondary syphilis, who died from extensive anomalies in the lungs while having severe arsphenamine dermatitis. The original diagnosis of syphilitic pneumonia was rejected because of the striking resemblance of the findings to those occurring in rheumatic pneumonia. It is considered that acute exudative syphilitic pneumonia has not been proved up to now and very probably does not exist; and cases so diagnosed represent allergic reactions in the lungs. G. A. H.

ALLERGIC CUTANEOUS VASCULITIS. M. Ruiter. (1952) *Acta derm.-venereol., Stockh.*, **32**, 274.

The general histology of allergic inflammation in general is discussed, and a case of cutaneous periarteritis nodosa is presented as an example of allergic vascular inflammation. The histological pictures of allergic vasculitis may differ depending on the nature and vehemence of the allergic reaction, the point of attack, the localization and the calibre of the vessels involved. It is suggested that various cutaneous anomalies exist in which the histology is dominated by allergic inflammatory processes of the blood vessels. Purpura Schoenleini should be considered primarily as an allergic vasculitis, the purpura being of secondary importance. The clinical picture and course of skin eruptions showing the picture of a haematogenous disseminated reaction is described and illustrated by examples. A syndrome is proposed of "allergic or allergic-hyperergic arteriolitis of the skin" in which the small vessels of the corium and particularly the arterioles are chiefly involved, showing fibrinoid necrosis, etc. G. A. H.

STUDIES ON THE ROLE OF LYMPHOCYTES IN ANTIBODY PRODUCTION. Tore Wesslen. (1952) *Acta derm.-venereol., Stockh.*, **32**, 265.

Lymphocytes in the form in which they enter the blood stream do not contain antibodies but are capable of producing them. The lymph plasma has a lower antibody titre than the blood serum. These conclusions are from experiments with thoracic duct lymph from animals immunized with *S. typhi* or horse serum. No bacteria were found in the lymph of animals infected with living *S. typhi*. G. A. H.

LUPUS ERYTHEMATOSUS DISSEMINATUS. L. M. Sonne and Michael Schwartz. (1952) *Acta derm.-venereol. Stockh.*, **32**, 333.

Four cases of disseminated lupus erythematosus treated with ACTH showed a dramatic disappearance of symptoms in three within a few days, but treatment had to be recommenced when the patients relapsed. The fourth patient showed no clinical effect, but a decrease in the globulin fraction in the blood and sedimentation rate with eosinopenia. Marked depression of the serum globulin occurred in all four cases. G. A. H.

EFFECTS OF MEPACRINE (ATABRINE). Franz Hermann and Otis B. Miller. (1952) *Acta derm.-venereol., Stockh.*, **32**, 317.

The skin of 9 patients examined *in situ* through a stereoscopic wide-field microscope under filtered ultra-violet light showed a bright canary-yellow fluorescence of the spiral portion of the sweat ducts during and after Atabrine ingestion. External application of Atabrine also produced

a bright fluorescence of the spiral part of the ducts. The terminal part of the sweat ducts is electrophysiologically negative. A positive charge drug such as Atabrine would be attracted to the terminal part of the ducts, diminishing electrophysiological potential along the ducts, and this results in stagnation of sweat and would serve to explain the decreased sweating caused by systemic administration of Atabrine. A patient with post-Atabrine sweat retention syndrome showed a peculiar fluorescence at the spiral portion of many of the remaining ducts some six years after the intake of the drug. G. A. H.

PHARMACOLOGIC AND PATHOGENETIC EFFECTS OF MEPACRINE CHLORIDE (ATABRINE) UPON THE HUMAN SKIN. Franz Herrmann and Otis B. Miller. (1952) *Acta derm.-venereol., Stockh.*, 32, 304.

Fluorescence is observed in the skin under filtered ultra-violet light after oral administration of mepacrine hydrochloride (Atabrine). During daily Atabrine administration and for a long time after a profuse jade coloured fluorescence was noticed in all the skin and mucous membranes of all test subjects. Intensity of fluorescence increased for some considerable period after the discontinuation of the drug. The fluorescence of specimens of various materials collected from the skin during and after the intake of Atabrine revealed a preponderance of the drug in the keratinous components and ether-soluble material and only occasional slight fluorescence in the sweat, but it is suggested that the sweating system plays a significant part in the distribution of the drug in the skin. Delayed and diminished delivery of sweat was observed in one individual during and after intake of the drug, and especially so in another volunteer who had developed lichenoid Atabrine dermatitis. G. A. H.

INCIDENCE, SIGNIFICANCE AND BACTERIOLOGICAL FEATURES OF PLEUROPNEUMONIA-LIKE ORGANISMS IN A NUMBER OF PATHOLOGICAL CONDITIONS OF THE HUMAN GENITO-URINARY TRACT. M. Ruiter and H. M. M. Wentholt. (1952) *Acta derm.-venereol., Stockh.*, 33, 130.

Eighteen strains of pleuropneumonia-like organisms were isolated partly from non-gonococcal urethritis in males and partly from vaginitis and cervicitis in females. The strains isolated are probably closely related and belonged to one and the same group. Instillations of the pleuropneumonia-like organisms isolated from non-gonococcal urethritis into the urethra of healthy males were without effect. The pathogenicity of pleuropneumonia-like organisms in man is improbable, but it is possible that under certain circumstances they may have a pathological significance. From 32 males suffering from non-gonococcal urethritis the organisms were cultured in 8 cases. Furthermore the organisms concerned could be isolated from 10 out of 14 women suffering from leucorrhoea. In the husbands of 4 women organisms morphologically and culturally like those found in the female patients could be shown. Two of these men suffered from non-gonococcal urethritis and the third from ordinary balanitis; the fourth was completely free of symptoms, the organism having been isolated from prostatic fluid. G. A. H.

ISOLATION OF A PLEUROPNEUMONIA-LIKE ORGANISM (G STRAIN) IN A CASE OF FUSOSPIRILLARY VULVOVAGINITIS. M. Ruiter and H. M. M. Wentholt. (1952), *Acta derm.-venereol., Stockh.*, 33, 122.

A pleuropneumonia-like organism was isolated in a 29-year-old woman with fusospirillary vulvovaginitis. The characteristics of this organism were similar to those of pleuropneumonia-like organisms, isolated previously in fusospirillary infections of the male genito-urinary tract (G-strain). G. A. H.

CRYPTOCOCCOSIS. F. Linell, B. Magnusson, and A. Norden. (1952). *Acta derm.-venereol., Stockh.*, 33, 102.

The first case of cryptococcosis observed in Sweden is described, the patient having four years' history of pulmonary lesions of unknown origin. Acneiform infiltrates appeared later suddenly to prove evidence of skin lesions. *Cryptococcus neoformans* was isolated from these lesions, from gastric washes and from cerebral spinal fluid. Treatment with sulphonamides and Terramycin failed to have any effect. G. A. H.

OXYURIDAE. Jorgen Christiansen. (1952) *Acta derm.-venereol., Stockh.*, 33, 97.

A study designed to show how many times it should be reasonable to repeat the investigation for eggs when oxyuridae are suspected. 43% of a total number of 1751 persons examined by the

N.I.H. swab technique were detected at a single examination, whether it was the first, second or third examination. After five negative examinations the chance of being infected is only 1·2%. G. A. H.

AN ERRONEOUS DIAGNOSIS OF OXYURIDAE. Jorgen Christiansen. (1952) *Acta derm.-venereol., Stockh.*, **33**, 94.

A patient with anal itch found two worms on her flannel after an anal toilet and an erroneous diagnosis of oxyuridae was made. The worm was a lumbricillus which frequently lives in hand basins, and is not parasitic. In all cases of oxyuris search for eggs should be made. G. A. H.

COMPARISON OF THE MAZZINI AND THE REIN-BOSSAK MICROFLOCCULATION SLIDE TESTS. I. Hesselberg and Tschudi Sigv Madsen. (1952) *Acta derm.-venereol., Stockh.*, **33**, 84.

The Mazzini and Rein-Bossak microflocculation slide tests in 5953 sera showed that both tests had a satisfactory sensitivity and high specificity. The Mazzini test is slightly more sensitive, but both reactions are of equal specificity. G. A. H.

RISK OF INFECTION BY SEXUAL INTERCOURSE WITH SYPHILITIC PARTNER. B. Schaffer and B. Sylvest. (1952) *Acta derm.-venereol., Stockh.*, **33**, 91.

Out of 50 people who had sexual intercourse with a syphilitic partner within the incubation period and/or in the first and/or second stage about half became infected with syphilis. The risk of infection was smaller when coitus had taken place exclusively within the incubation period (between one-fourth and one-third were affected) than when the partner had syphilitic skin or mucous manifestations, when some two-thirds were infected. G. A. H.

TUBERCULIN SENSITIVITY IN ERYTHEMA INDURATUM. Georg Seeberg. (1952) *Acta derm.-venereol., Stockh.*, **33**, 73.

In 13 patients with erythema induratum the Mantoux test was done on the lower leg near the active lesions, and in the normal skin of the thigh and the upper arm. The reactions in the lower leg showed the greatest intensity and the longest duration. The arm reactions were weakest and briefest. In ten patients the lower leg reactions produced a clinical appearance identical with that of erythema induratum. The variations in the reactions in the different sites would appear to be compatible with the presence of a higher titre of antibodies in the vicinity of the lesions and may provide possible evidence of tuberculous aetiology. G. A. H.

THE OCCUPATIONAL SIGNIFICANCE OF SOME COMMON CONTACT ALLERGENS. Erik Skog and Nils Thyresson. (1952) *Acta derm.-venereol., Stockh.*, **33**, 65.

3287 eczema patients were patch-tested to common allergens (chromium, formalin, nickel sulphate, turpentine and para-phenylendiamine). 31·1% of women and 32·5% of men gave positive reactions. The order of frequency of positive reactions was formalin, chromium, nickel, sulphate, turpentine and para-phenylendiamine in this order. G. A. H.

SKIN SENSITIVITY TO DIFFERENT TERPENES AND TERPENE FRACTIONS. Sven Hellerstrom and Nils Thyresson. (1952) *Acta derm.-venereol., Stockh.*, **33**, 51.

Patch tests were done on patients sensitive to turpentine to determine the sensitizing power of (*a*) purified terpene, (*b*) terpene oxidation products, and (*c*) chemical substances isolated from oxidized turpentine. The intensity of the cutaneous reaction is consistent with the degree of oxidation of the terpenes, and even persons hypersensitive to terpene do not react to pure terpenes. On displacement adsorption, terpenes can be split into eczematogenically active and inactive constituents. It is probable that the eczematogenically active substances have uniform configuration in the various turpenes. G. A. H.

ON THE VARIABILITY AND CLASSIFICATION OF DERMATOPHYTES. Heiti Paldrok. (1952) *Acta derm.-venereol., Stockh.*, **33**, 1.

The previous classification of fungi has been revised by the author whose new classification is based on the morphological characteristics of the fungi grown on artificial media. Three intergrading main stages are recognized: (1) stage with complete morphology (florentiform stage); (2) stage with cottony tuft, consisting of hyphae, developing scanty micromorphologic structures

in retrogressive stage or sterile hyphae only (rubriform stage); (3) stage of glabrous or faviform colonies (faviform stage). All the dermatophytes are considered to belong to one genus only, which on account of the priority of the name has to be called Microsporum. There are only three species: *Microsporon audouini* (formerly *Microsporon canis*), *Microsporon gypseum* and *Microsporon tonsurans* (*Trichophyton mentagrophytes*). All other types are more or less degenerative stages. The stages coincide with the clinical manifestations caused by fungi. The strains with complete morphology (first florentiform stages) caused classical, well circumscribed forms of tinea. The strains of the second stage (rubriform) caused more chronic and eczematous lesions and strains of the faviform stage caused the clinical picture known on the whole as favus. Routine cultivation of fungi should be done with uniform medium, best with Sabouraud's glucose-agar.

G. A. H.

LOCAL OXYTETRACYCLINE ("TERRAMYCIN") THERAPY OF SKIN INFECTIONS. Carroll S. Wright and Donald N. Tschan. (1953) *Arch. Derm. Syph., Chicago*, 67, 125.

The authors report very satisfactory results with terramycin ointment, especially in impetigo. Folliculitis and sycosis vulgaris and impetigenized miscellaneous eruptions were also, in most cases, cured, though more slowly. Unfortunately the article is marred by the authors' failure to mention the strength of the ointment used or how often applied, except in impetigo, when "it was rubbed in gently but thoroughly every 3 hours," presumably by day only. In the text it said that virus diseases were unaffected, but in the table one case of Kaposi's varicelliform eruption is listed as cured in 72 hours. Of 635 patients treated 391 had various dermatoses and 244 had minor surgical wounds which all healed satisfactorily with terramycin. In no case did terramycin cause irritation of the skin, though in 4 there was irritation due to the ointment base.

J. K.

AQUEOUS SOLUTIONS OF SODIUM PROPIONATE WITH CHLOROPHYLL AS A THERAPEUTIC AGENT. Samuel M. Peck, Eugene F. Traub and Herbert J. Spoor. (1953) *Arch. Derm. Syph., Chicago*, 67, 263.

The authors strongly advocate the use of a solution of 1% sodium propionate and 0·0025% sodium copper chlorophyllin (the strength may be increased) as a moist dressing, foot bath, mouth wash or douche in the acute stages of dermatitis and eczema, intertrigo, monilia infections, etc. The chlorophyll not only counteracts the odour of the sodium proprionate but enhances its therapeutic effect.

J. K.

VITAMIN A INTOXICATION. E. Bifulco. (1953) *New Engl. J. Med.*, 248, 690.

Vitamin A intoxication in an adult who had received 100,000 i.u. daily for four years is reported. Signs and symptoms included loss of weight, loss of hair, pain in the joints, tenderness of the extremities, exophthalmos, haemorrhages from mucous membranes, a low red cell count and eosinophilia.

A. D. P.

PLANTAR WARTS; CURE BY INJECTION. Capt. E. C. Branson and Col. R. L. Rhea, Jr. (1953) *New Engl. J. Med.*, 248, 631.

Two to three c.c. of 1% novocain are injected into the base of the wart under pressure, so that it is raised and the surrounding skin is blanched. Seven days later the wart can generally be picked out with forceps, though occasionally one or two further injections may be required.

A 26 gauge needle and Luer Lock dental syringe are recommended.

Of 48 patients so treated 73% were cured and 96% relieved of symptoms.

A. D. P.

NEVUS UNIUS LATERALIS. N. Lenson. (1953) *New Engl. J. Med.*, 248, 757.

The possibility of carcinoma developing in patients suffering from naevus unius lateralis is emphasized in the report of a case associated with abnormalities of the bones and mucous membranes of the mouth and nose.

A. P. D.

THE EFFECTS OF THE RESIN OF EUPHORBIA ON VERRUCAE PLANTARES IN HUMAN AND ANIMAL EXPERIMENTATION. R. W. Goldblum and A. C. Curtis. (1953) *J. invest. Derm.*, 20, 45.

The Arabs use the resin as a veterinary vesicant and cathartic; and the milky juice is of course a traditional home remedy for warts. Of 60 cases a cure was obtained in 58. The changes were shown histologically to be similar to those produced by podophyllin.

How difficult it is to assess the value of a wart-cure, and especially without a control series ! The reviewer's own experiments with Lewisite convinced him that the most impressive treatment is of no avail in the hands of an unbeliever, and yet how many apparently inert remedies have been reported to cure ! J. H. T. D.

A HAEMOLYTIC SEROLOGIC REACTION WITHOUT COMPLEMENT AS A POSSIBLE TEST FOR SYPHILIS. H. A. Cohen. (1953) *J. invest. Derm.*, **20**, 5.

To those who have felt the need to understand the Wassermann reaction this study will no doubt appeal. In an old packet of dried egg was discovered something which was both haemolytic and had an affinity for the reagin present in syphilitic serum. Unfortunately fresh supplies of the same brand of egg powder did not contain it. J. H. T. D.

THE METAL CONTENT OF SKIN, NAILS AND HAIR. R. W. Goldblum, S. Derby and A. B. Lerner. (1953) *J. invest. Derm.*, **20**, 5.

Spectrographic analysis of pooled specimens of skin, hair and nails from 18 normal white males whose ages ranged from 15 to 70 revealed the presence of a large assortment of elements. The attempt is made to classify them according to whether they are known to have a metabolic function or to be associated with enzymes or not. Great individual variations, as might be expected, were found, and it occurs to the reviewer that it would have been more instructive to compare the quantities of some of the " inert " metals in the suckling crawler and dotard. J. H. T. D.

EXAMINATION OF THE EPIDERMIS BY THE STRIP METHOD. II: BIOMETRIC DATA ON REGENERATION OF HUMAN EPIDERMIS. H. Pinkus. (1952) *J. invest. Derm.*, **19**, 431.

Elaborate confirmation of previous work (*J. invest. Derm.*, **16**, 383), designed to show that the basal layer is the main locus of epidermal regeneration and that the stimulus is removal of keratinized layers. J. H. T. D.

ELECTRON MICROSCOPY OF NORMAL HUMAN SKIN. M. Gray, H. Blank and G. Rake. (1952) *J. invest. Derm.*, **19**, 449.

Ordinary microphotographs may help to recall some of the details of stained sections. These electron photographs of sections said to be no more than 0·1μ thick represent phenomena incapable of direct visual experience : but they convey what might be expected of great magnification, namely chaos and a fortuitous concourse of atoms. Attention is drawn to some good qualities of osmic acid. J. H. T. D.

A STUDY OF ECZEMATOUS SENSITIVITY TO FORMALDEHYDE. A. Rostenberg, B. Bairstow and T. W. Luther. (1952) *J. invest. Derm.*, **19**, 459.

Four nurses, through having to handle thermometers kept in 10% formaldehyde, became sensitized and developed eczematoid dermatitis of the fingers. When the practice was stopped the trouble entirely disappeared. On patch testing, reactions were not obtained with any dilution higher than 1 : 200 and some of them were not evident before 72 hours. Reactions were negative to other aldehydes in common use. Attention is drawn to reports of immediate wheal reactions and to eczematoid reactions with dilutions as high as 1 : 8,000,000—in which state of dispersion of the relevant molecules anything might happen, of course. J. H. T. D.

SODIUM PARA-AMINOBENZOATE (" PABA ") IN THE TREATMENT OF DERMATOSES. L. D. Grayson and K. Steiner. (1952) *J. invest. Derm.*, **19**, 463.

A failure to confirm the claims of Weiner (1950) and Loewenthal (1951), by investigators who naively admit they still hope to cure " certain types of dermatoses which improve spontaneously on hospitalization and show irregular remissions " with something out of a bottle.

If it won't work when taken by the mouth then we have other ways of giving it : perhaps, they say, the doses were too large—too small maybe. Anyhow, PABA has much in common with ACTH, which in turn has something that reminds us of Tacitus's appreciation of Galba. J. H. T. D.

THE THRESHOLD OF SKIN FLARE IN PERSONS WITH AND WITHOUT MALIGNANT NEOPLASTIC DISEASE. F. B. Benjamin and A. C. Ivy. (1952) *J. invest. Derm.*, **19**, 467.

The discovery of any physiological difference between persons suffering from cancer and those

who are not will always seem to promise another chance of attacking the disease. Patients with advanced or metastatic cancer require a stronger thermal stimulus to produce a flare.

J. H. T. D.

EXPERIMENTAL THERAPY OF CHRONIC PORPHYRIA WITH VITAMIN B_{12}. C. J. Dillaha and W. Hicklin. (1952) *J. invest. Derm.*, **19**, 489.

Provided that the patient will abstain from alcohol, vitamin B_{12} has some effect in reducing the output of porphyrin; and the hypertrichosis, pigmentation and blisters on the backs of the hands tend to diminish. There is a picture of a lady "before and after." We would have taken their word for it, but when we come to think of it, how do we know she hasn't had a shave ?

J. H. T. D.

SPECIFIC TISSUE ALTERATION IN LEPROUS SKIN. II: THE HISTOLOGY OF THE TUBERCULIN REACTION IN LEPROSY. F. Sagher, E. Kocsard and E. Liban. (1952) *J. invest. Derm.*, **19**, 499.

The histology of the tuberculin reaction in the skin of lepers simulates that of the specific lesions of lepromatous leprosy, except that of course bacilli are not to be seen. J. H. T. D.

ALLERGIC FACTORS IN THE PRODUCTION OF LEUKAEMIDS. R. W. Goldblum, F. C. Bocobo and A. C. Curtis. (1953) *J. invest. Derm.*, **20**, 1.

The name leukaemid is commonly used for any efflorescence occurring in leukaemia that cannot be shown to contain cellular elements specific to the disease. These rashes, etc., have in the past been attributed to toxins derived from the metabolism of perverted tissues or have been supposed to represent a non-specific tissue reaction against tumour cells—the idea of course being that such cells are in some way foreign to the organism. The subject is of great interest, because not only does the skin react nonspecifically in a great variety of untidy rashes, but clinical entities such as varicella and lichen planus are occasionally observed to take a significant though perhaps a fugitive hand in the systemic disease.

For these reasons the present work merits our attention and we look forward to its continuation. So far the results are not very conclusive ; but we hope the authors will not fail to let us know if anything untoward happens to the control subjects, some of whom had serum or cells from leukaemic patients injected into their skin. J. H. T. D.

SARCOMA OF THE SKIN. A. Steppert and S. Wolfram. (1952) *Arch. Derm. Syph., Berl.*, **193**, 566.

A clinical account, with photographs and histology, of 6 cases from the Vienna clinic. One was a fibrosarcoma, four were reticulosarcomata, the sixth a primary lymphosarcoma of the skin.

M. F.

LUPUS ERYTHEMATOSUS CELLS. X. Vilanova. (1952) *Arch. Derm. Syph., Berl.*, **193**, 598.

Vilanova had 5 acute and 5 subacute cases of L.E. available for study in the course of 2 years in his department in Barcelona. L.E. cells were found in 3 acute and one subacute case.

M. F.

FOREIGN-BODY GRANULOMA AND SARCOID. W. Gahlen and N. Kluken. (1952) *Arch. Derm. Syph., Berl.*, **194**, 121.

Two further cases in which sarcoid developed at the sites of blast injuries sustained during the war. The latent periods were five and eight years respectively, Lung changes were present in both. M. F.

MORPHOLOGY OF HEALTHY AND DISEASED SKIN. E. Horstmann. (1952) *Arch. Derm. Syph., Berl.*, **194**, 164.

Epidermis was separated from connective tissue by maceration. The undersurface of the epidermis could be studied, and interesting photographs of the various reliefs obtained are presented. M. F.

INVESTIGATION OF THE ACTION OF PENICILLIN. W. Blaich and M. Fiene. (1952) *Arch. Derm. Syph., Berl.*, **194**, 174.

In the rat prolonged administration of penicillin appears to activate the thyroid. Furthermore the vitamin C content of the suprarenal cortex is reduced by 15% after 3 weeks' treatment with penicillin. M. F.

ECZEMA OF THE HANDS. J. Gomez Orbaneja and P. A. Quinones Caravia. (1952) *Actas dermo-sif., Madrid*, **43**, 747 ; **44**, 101 and 161.

Eczematous rashes on the hands are common. The authors found 290 examples of it in 2600 patients and have tried to correlate the various clinical types with particular pathogenic mechanisms.

Type I : Essentially erythemato-congestive lesions cover the whole of the back of the hand and often the backs of the fingers and wrist and in half the cases extend on to the forearms. The rash is often obstinately chronic.

Type II : Involvement of the most prominent parts, e.g., the backs of the metacarpo-phalangeal and inter-phalangeal joints and the cubital border of the hand. The elementary lesions vary in type ; the right hand is usually affected alone and external factors are usually important.

Type III : The interdigital folds and spaces, extending somewhat on to the palm, often sharply marginated red eroded lesions. Often of parasitic origin and may also have lesions elsewhere, e.g., toes. Usually respond rapidly to appropriate treatment.

Type IV : Isolated lesions, generally vesicopapular—repeated sudden eruptions—little influenced by local treatment.

Type V : Patches of various kinds. Only improved but rarely cured with local treatment. The essential factor is generally some form of sensitization.

Type VI : Patches more or less limited to the fingers, and when at the distal end are frequently bullous.

Type VII : Vesico-bullous lesions, coming out in crops, usually on thenar and hypothenar eminences, may also have similar lesions on the sides of the fingers and occasionally on the backs of the hands. This type is nearly always associated with some focus of infection in the skin or elsewhere.

Type VIII : Hyperkeratotic lesions confined to the palms. At times may be difficult to distinguish from psoriasis. Mycotic infection the most frequent cause, some mechanical contact is also not infrequently the origin.

Type IX : The whole of the palm is affected, sometimes redness with exaggeration of the normal creases. Often in middle-aged hard-working women whose hands are irritated by prolonged contact with various non-specific substances and sometimes a manifestation of the climacteric.

Type X : Hyperkeratotic lesions scattered irregularly over the palm. Often due to contact, flexion of the palms protecting certain areas.

Of 200 cases studied in detail 138 had persisted for longer than 6 months and 103 of them for over 2 years. Eczema due primarily to irritants was more common in women. The authors think that allergy to some infection or of alimentary origin is responsible for the persistence of many lesions—e.g., in Type II only 2 of 10 patients improved when the treatment was restricted to dressings protecting the skin from all external irritants. G. W. B.

THORIUM X IN THE TREATMENT OF ALOPECIA AREATA. H. T. Wilson. (1952) *Arch. Middlesex Hosp.*, **2**, 239.

The author treated 36 patients suffering from alopecia areata by painting monthly half the bald area with thorium X—1500 e.s.u. per c.c. of *n*–propyl alcohol and the other half with industrial methylated spirit. After from 3 to 18 applications 17 patients had no regrowth of hair. In the rest the hair was largely or entirely restored, 4 of them showing no appreciable difference between the treated and control halves : 3 had a thicker growth on the treated side and in 12 regrowth was accelerated on that side. In 4 patients the regrowth was short lived. In a control series of 40 patients who had been treated with a simple stimulating lotion 27 replied to a questionary : 22 had recovered completely and 3 partially, so it is evident that although painting with thorium X often accelerates regrowth of hair, the end-result is not much better than with simpler methods of treatment. G. W. B.

PSEUDO-DENDRIFICATION IN EPITHELIAL CELLS OF THE EPIDERMIS. Eugenia Follman and Marcial I. Quiroga. (1952) *Rev. argent. Dermatosif.*, **36**, 217.

When studying dendritic cells in melanogenesis by silver impregnation methods the authors could by modifying their staining technique transfer all the basal layer and growing epithelial cells into typical dendritic ones. They believe a dendritic cell to be an ordinary basal cell that has become altered by some agency, and that human epidermis consists of only one type of differentiated epithelial cell from which through congenital pathological or artificial means secondary atypical cells of the most varied form and size can be formed. G. W. B.